ABSTRACTS OF WORLD MEDICINE

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Pathology

1071. **Experimental Measles in Young Dogs.** (Экспериментальная корь у щенят)
N. E. RYAZANTSEVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 22–29, No. 5, May, 1956. 2 figs.

After 48 young dogs had been infected with material from patients with measles a rise of temperature was observed in 50% and hyperaemia of the mucous membranes and a measles-like rash in 38%. Measles virus was present in the blood of all the dogs between the 2nd and 8th days after infection. The infection could be passed on to other young dogs by injecting blood from the infected animals subcutaneously and by introducing it simultaneously into the nose and on to the conjunctivae and buccal mucosa. Sometimes an increase in the severity of the symptoms followed this passaging. Agglutinating and neutralizing antibodies against strains of the virus from dogs, monkeys, and man were present in the blood of the infected dogs from the 28th day after infection.

[This paper confirms the findings of two similar investigations previously reported by Russian authors. The demonstration that the infection is transferable to an easily available—and inexpensive—experimental animal is of considerable importance for research in this field.] *K. Zinnemann*

CHEMICAL PATHOLOGY

1072. **A Comparative Study of Cerebrospinal Fluid and Serum Proteins in Multiple Sclerosis with Special Reference to the Lange Colloidal-gold Reaction**
E. M. PRESS. *Biochemical Journal* [*Biochem. J.*] 63, 367–372, 1956. 4 figs., 23 refs.

Positive Lange colloidal-gold reactions in the cerebrospinal fluid (C.S.F.) in cases of disseminated sclerosis have been variously reported as occurring in 29 to 81% of cases. At the Middlesex Hospital, London, the author examined the protein pattern in serum and C.S.F. from patients with disseminated sclerosis by means of microelectrophoresis and found in some cases an increase in the γ-globulin concentration in the C.S.F., but not in the serum, to be associated with a positive Lange colloidal-gold reaction. The origin of the increased γ-globulin content of the cerebrospinal fluid is not known. It was further shown that albumin and α and β globulins isolated by continuous paper electrophoresis from serum and C.S.F. in such cases inhibited coagulation of the colloidal-gold sol, whereas γ globulin coagulated the sol. The proteins of the C.S.F. were similar to serum proteins, except that the more rapidly sedimenting components of serum α globulin were not detected in C.S.F. and also that α globulin from the C.S.F. was a stronger inhibitor of colloidal-gold sol coagulation than was serum α globulin. An additional protein, " Component S ", was found in the β- and γ-globulin fractions of the C.S.F. This component was not precipitated by 18% sodium sulphate, had a low sedimentation constant (about 2 Svedberg units) and inhibited the colloidal-gold reaction. The significance of " Component S " is discussed.
J. E. Page

1073. **The " Corrected " Bromsulfalein Test. A Comparison with the Cephalin–Cholesterol Flocculation Test and the Thymol Turbidity Reaction in Jaundiced Patients**
C. METZLER, F. W. HOFFBAUER, and E. BENSON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 47, 519–528, April, 1956. 2 figs., 8 refs.

The " bromsulphalein " retention test is not usually considered to give valid results in the presence of jaundice. In 1951 Zieve *et al.* (*J. Lab. clin. Med.*, 1951, 37, 40) claimed to have obtained useful results with a correction factor by which the value obtained was related to the plasma bilirubin level. The present authors, in a study at the University Hospital of Minnesota, Minneapolis, have evaluated the usefulness of the corrected test in 111 jaundiced patients. They conclude that even with the correction factor the test gives erratic results and is inferior to the simpler flocculation tests in the differential diagnosis of jaundice. *P. C. Reynell*

1074. **Bilirubin–Protein Linkages in Serum and their Relationship to the van den Bergh Reaction**
G. KLATSKIN and L. BUNGARDS. *Journal of Clinical Investigation* [*J. clin. Invest.*] 35, 537–551, May, 1956. 9 figs., 33 refs.

Serum containing bilirubin may give a direct reaction in the van den Bergh test or may have to be treated with alcohol and ammonium sulphate before doing so. The most widely accepted explanation is that of Watson (*Blood*, 1946, 1, 99), who suggested that indirect-reacting bilirubin is a stable globulin complex derived from haemoglobin, from which bilirubin is split off in the liver and excreted in the bile as a sodium salt which gives the direct van den Bergh reaction. In obstructive conditions this direct-reacting bilirubin is regurgitated into the blood, where it is loosely bound by albumin but con-

tinues to react directly. The investigation reported here from Yale University School of Medicine was carried out to re-evaluate conflicting evidence concerning the existence in the blood of such a compound as bilirubin–globulin, filter-paper electrophoresis being the principal method employed and blood from patients with various types of jaundice being examined.

It was found that virtually all bilirubin in the serum is bound to albumin, whether it gives a direct or an indirect van den Bergh reaction; if there exists any bilirubin–globulin at all it cannot account for more than 0·05 mg. of pigment per 100 ml. of serum. Both types of bilirubin are firmly bound to albumin at *p*H 6 to 9 and separate from it below *p*H 5. As the van den Bergh reaction is usually carried out at *p*H 2 to 4 it must be assumed that both types of bilirubin are in an unbound state when they react with the diazo reagent. The results of this investigation support strongly the work of Cole and Lathe (*J. clin. Path.*, 1953, **6**, 99), who have shown that the two types of bilirubin can be separated by reverse-phase chromatography and differ in their solubility in water. *H. Lehmann*

1075. **The Relation of Blood Pepsin to Gastric Secretion with Particular Reference to Anacidity and Achylia**
H. M. Spiro, A. E. Ryan, and C. M. Jones. *Gastroenterology* [*Gastroenterology*] **30**, 563–579, April, 1956. 8 figs., 16 refs.

The relationship between the blood pepsin level and gastric secretory activity, with particular reference to achlorhydria, was studied in 400 patients at the Massachusetts General Hospital, Boston, and Grace–New Haven Community Hospital, New Haven, Connecticut. A " reasonably good straightline relationship " between the blood pepsin level and the gastric pepsin concentration was observed in 38 patients with free acid in the stomach; this was not found in 12 patients without free acid. A lack of parallelism was also noted after insulin stimulation in 6 patients with duodenal ulcer, the gastric pepsin concentration rising over 100% while the blood pepsin level rose only 10%. It proved difficult to establish any close correlation between the blood pepsin content and the gastric *p*H before and after histamine.

Four different groups were distinguished among patients with a clinical diagnosis of achlorhydria: (1) achlorhydria with achylia; (2) achlorhydria without achylia; (3) clinical achlorhydria; and (4) false achlorhydria. Achylia (blood pepsin level below 120 units) was present in only 10 of the 400 patients. The second and third groups were distinguished by the complete absence in the former of any fall in gastric *p*H on giving histamine. In all such cases the blood pepsin level was below 350 units, whereas when a response to histamine was present the level was considerably higher. A high blood pepsin level was found in cases of false achlorhydria due to oesophageal stricture or subtotal gastrectomy.

Various extragastric factors affected the blood pepsin level. In 15 uraemic patients, 5 diabetics treated with depot insulin, 6 patients with acute myocardial infarction, and 6 with hyperparathyroidism it was uniformly raised. The authors point out that in interpreting the results of the blood pepsin determination it is particularly important to be sure that renal function is normal. The highest average blood pepsin level was found in patients with duodenal ulcer; in most of the 116 such cases in the series the level was higher than 450 units. Moreover, after partial gastrectomy it was higher in patients with duodenal ulcer than in those with gastric ulcer.

The authors finally discuss the relationship between acid secretion and the blood pepsin and uropepsin concentrations and the value of determining the blood pepsin level in gastric cancer precursor surveys.

P. I. Reed

HAEMATOLOGY

1076. **Nucleophagocytosis. Studies on Three Hundred Thirty-six Patients**
P. Heller and H. J. Zimmerman. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 403–408, April, 1956. 4 figs., 23 refs.

The significance of nucleophagocytosis was studied at the University of Illinois College of Medicine, Chicago, in 336 patients, the L.E.-cell test being performed in all cases by the method of Zimmer and Hargraves. The authors state that in accordance with the nomenclature suggested by Hargraves the term " tart " cell refers to a phagocytic monocyte. The engulfing cell, when a polymorphonuclear leucocyte, is called a Type-A cell if the engulfed nucleus shows a well-preserved chromatin pattern and a Type-B cell if it does not. The Type-B cell resembles the L.E. cell, but the engulfed nucleus does not have the smoky appearance of the L.E. inclusion body and usually has a basophilic rim. It is not associated with rosette formation.

The Type-B cell was found in fewer than 5% of healthy subjects and of patients with various diseases for which they were not receiving penicillin. Administration of penicillin did not result in an increase in the incidence of such cells unless there was an associated allergic reaction. Type-B cells were found in sera from 14 out of 43 patients giving an allergic reaction to certain drugs. In 2 patients L.E. cells and rosettes were transiently demonstrated. Type-B cells were always seen in sera from patients with systemic lupus erythematosus, even when L.E. cells were not detectable. Tart cells and Type-A cells have no clinical significance.

E. G. Rees

1077. **The Action of Heparin in the Prevention of Prothrombin Conversion**
A. S. Douglas. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 533–536, May, 1956. 22 refs.

The coagulation of blood proceeds in three stages: (1) antihaemophilic globulin, platelets, and Christmas factor (P.T.C.), with the assistance of Factor V (labile factor) and Factor VII (proconvertin) react to form thromboplastin; (2) this compound catalyses the conversion of prothrombin into thrombin; (3) thrombin

enables fibrinogen to be converted into fibrin. It is generally accepted that the anticoagulant effect of heparin is due to an interference with the reaction of thrombin with fibrinogen. The present investigation was undertaken at the Royal Infirmary, Glasgow, with a view to finding out whether heparin also interferes with the earlier links in the coagulation chain.

Normally, antihaemophilic globulin and Factor V disappear during the clotting of blood samples, presumably because they are used up in Stage 1. However, assays carried out on blood taken from 9 patients before and 5 minutes after the intravenous injection of 10,000 units of heparin and allowed to clot showed that in the presence of heparin neither of these two substances disappears, and this is taken as evidence of an interference by heparin with Stage 1. A consequent inability to convert prothrombin to thrombin in the presence of heparin could also be demonstrated. The author suggests that in fact the main action of heparin as an anticoagulant may not be to inhibit Stage 3, but to interfere with the utilization of thromboplastin precursors in Stage 1 and thus to prevent the conversion of prothrombin into thrombin in Stage 2. *H. Lehmann*

MORBID ANATOMY AND CYTOLOGY

078. **Thrombotic Microangiopathy**
V. St. C. Symmers. *Lancet* [*Lancet*] **1**, 592–596, May 5, 1956. 3 figs., bibliography.

The clinical diagnosis of thrombotic microangiopathy is usually suggested by the development of a characteristic tetrad—acute febrile illness, haemolytic anaemia, thrombocytopenic purpura, and neurological disturbances. If thrombotic microangiopathy is to be recognized early the clinician must consider it in the differential diagnosis of every illness presenting with any of the components of the tetrad. The author of this paper from Charing Cross Hospital Medical School, London, points out that at present only biopsy offers any hope of providing confirmatory evidence of the diagnosis, but that this procedure has hitherto played little part in the study of the disease. Discussing the choice of tissue for biopsy he states that rib biopsy may prove to be the procedure of choice and that it could be combined with biopsy of the skin and muscle through the same incision. Particular care is required on the part of the pathologist to reduce to a minimum the delay occasioned by decalcification; careful dissection is necessary because the thrombotic lesions are most numerous in the zone of the marrow cavity immediately beneath the cortex. As regards treatment of thrombotic microangiopathy, which at present can only be empirical, there is some slight evidence that splenectomy may influence the course of the disease. Other methods of treatment have been without effect.

The author describes in detail 3 cases in which the diagnostic histological changes of thrombotic microangiopathy were found in surgical specimens (lymph node, uterine curettings, and appendix) before the clinical syndrome developed. *A. W. H. Foxell*

1079. **The Histology of the Cutaneous Manifestations of Systemic Lupus Erythematosus.** (Histologie des manifestations cutanées du lupus érythémateux systématisé)
M. Prunieras. *Presse médicale* [*Presse méd.*] **64**, 772–776, April 25, 1956. 16 figs. 40 refs.

Degradation of deoxyribonucleic acid in the nuclei of cells, with the formation of the so-called " red bodies ", was demonstrated histochemically in sections of normal skin subjected to the action of depolymerizing agents and of the skin of patients with systemic lupus erythematosus not so treated. This phenomenon affects mainly the nuclei of lymphocytes and is then non-specific, occurring also in the discoid form of lupus erythematosus and in other conditions such as lichen planus and dermatomyositis. " Red bodies " derived from connective tissue cells, however, appear to be specific to systemic lupus erythematosus, and are related to the L.E.-cell phenomenon.

Other histopathological changes in the skin in lupus erythematosus discussed in this paper are: (1) the increased metachromasia to toluidine blue of the vascular walls, basal membranes (especially around the hair follicles), and of the basal substance, especially in the dermal papillae; staining with periodic-acid–Schiff reveals changes in the same situations; (2) the swelling and disruption of the basal membranes; and (3) an increased phagocytic activity, especially on the part of histiocytes. The author appears to be of the opinion that the so-called fibrinoid necrosis is a product, not of collagenous degeneration, but of nuclear degradation. *A. Swan*

1080. **The Histopathology of Epidemic Follicular Keratosis**
H. I. Lurie and L. J. A. Loewenthal. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 120–127, April, 1956. 4 figs., 4 refs.

The authors, writing from the South African Institute for Medical Research, Johannesburg, describe the evolution, morphology, and subsidence of the lesions in epidemic follicular keratosis, as observed in a widespread outbreak of the disease in South Africa in 1954 and 1955. Examination of biopsy specimens taken at various stages of the eruption showed that 24 hours after the appearance of the rash there is recent extravasation of erythrocytes around the dilated hair follicles, together with mild intracellular oedema of occasional prickle cells and of endothelial cells of blood vessels. The last-named feature increases over the next 2 days and in some cases may go on to fibrinoid necrosis of the vessel wall and inflammatory cell infiltration. These vascular changes may be responsible for the oedema of the upper dermis which then ensues and interferes with the nutrition of the overlying epidermis. This degenerated epidermis may rupture under the pressure of the oedema fluid. Later, the inflammatory changes and haemorrhage round the hair follicles interfere with keratinization, and parakeratosis results, with accumulation of keratin in the mouth of the follicles, thus giving rise to the horny thorns from which the disease derives its name; in some cases a larger keratotic mass produces a comedo-like lesion.

In a brief discussion of the literature the authors point out that none of the previous workers refers to the prominent perivascular infiltrate or the vascular changes followed by haemorrhage or thrombosis described above and therefore suggest that the South African epidemic represents a form of the disease distinct from those previously reported. Its exact nature, however, remains uncertain, but histopathologically the picture is compatible with a virus or rickettsial infection or with an antigen–antibody reaction. *F. Hillman*

1081. **Response of Bone to Tumor Invasion**
R. A. MILCH and G. W. CHANGUS. *Cancer* [*Cancer (Philad.)*] **9**, 340–351, March–April, 1956. 3 figs., bibliography.

The authors present a review of the histopathology of metastatic bone tumours as seen in 241 cases studied post mortem at the Memorial Center for Cancer and the Sloane-Kettering Institute, New York, among which carcinoma of the breast, lung, and prostate, neuroblastoma, leukaemia, Hodgkin's disease, and myeloma were the most frequent types of primary tumour. A particular study was made of the response of bone tissue to the tumour, the presence of osteoblasts, osteoclasts, areas of osteoid formation, cartilaginous metaplasia, and connective-tissue proliferation being especially looked for.

The authors show that there is no essential difference, so far as the host bone is concerned, between "osteolytic" and "osteoblastic" metastases; the histological appearances in both cases differ only in a quantitative sense, the differences in bone response being only of degree and not of kind. For each case studied the relative proportions of bone-destroying and bone-producing elements were assessed by assigning a "grade of response" on a 5-grade scale in which Grade 0 represented destructive lesions and Grade 4 productive lesions. The number of cases showing the various grades of response are tabulated for each of the main types of tumour. Lesions assessed as Grade 0 (107) and Grade 1 (58) constituted approximately two-thirds of the total series of cases, and included virtually all the lesions described radiologically as osteolytic tumours. Grade-4 lesions included 9 cases of carcinoma of the breast, 9 of carcinoma of the prostate, one each of carcinoma of the thyroid, lung, oesophagus, and colon, one of neuroblastoma, 3 of plasma-cell myeloma, and one of malignant tumour of unknown origin.

In practically all the cases studied the bone destruction was regarded as resulting from the direct action of the tumour cells, or from pressure exerted by them, and not from active osteoclasis. Bone production on the other hand was the result of the proliferation of existing osteogenic cells or metaplasia of other connective-tissue cells: no evidence was found to suggest that the tumour cells were themselves osteogenic. Bone formation, and consequently the radiological opacity of a lesion, is regarded as bone healing, and therefore is taken as evidence of diminished growth of the tumour and not —as has been sometimes suggested—as evidence of increased growth activity of the tumour tissue. Active tumour growth and correspondingly pronounced bone destruction are regarded as the basis of the "osteolytic" type of lesion. *H. A. Sissons*

1082. **The Histological Diagnosis of Undifferentiated Tumours in Bone**
T. F. HEWER. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **7**, 230–236, April, 1956. 13 figs., 3 refs.

The problems of histological diagnosis encountered in a study of cases of reticulosarcoma, neuroblastoma, malignant synovioma, and Ewing's tumour are discussed, with reference to cases so classified in the Bristol Bone Tumour Register. These tumours, which the author groups together as "undifferentiated" or "round-cell", were present in 42 out of a total of 177 cases of "primary or secondary sarcomatous tumours" of bone. There were 14 cases of reticulosarcoma, the growth in 6 being primary in one bone; reticulin fibres were conspicuous and formed a diffuse network between the tumour cells. Synoviomata were diagnosed in 7 cases, but involved the bone in only 4; in addition to round-celled areas they showed spindle-celled tissue and clefts lined with endothelial cells. The series included 11 proven cases of neuroblastoma involving bone secondarily. The rosette was the diagnostic histological feature, but it was not always conspicuous. In 10 cases the growth was originally regarded as an example of Ewing's tumour, but in 5 this diagnosis had to be discarded because of insufficient evidence. Further study of the remaining 5 cases revealed a reticulosarcoma in one case, metastatic carcinoma in one, and secondary neuroblastomata in 3 cases.

The author considers that in cases of this kind the classification "Ewing's tumour" should be abandoned and that it is preferable provisionally to diagnose undifferentiated round-celled tumour until the proper diagnosis can be established from recognizable histological features. *H. A. Sissons*

1083. **The Grading of Osteogenic Sarcoma, and its Bearing upon Survival and Prognosis**
C. H. G. PRICE. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **7**, 237–241, April, 1956. 4 figs., 8 refs.

In this paper from the University of Bristol the author describes a method employed in grading 66 osteogenic sarcomata which depends on the assessment of the "mitotic ratio" (M.R.) of each tumour. The frequency of mitosis is determined in areas of homogeneous viable cellular tumour tissue, usually near the growing edge, the ratio being expressed as the number of resting nuclei relative to each mitosis. For the whole series of cases the average mitotic ratio was approximately 240:1. Three grades of osteogenic sarcomata were adopted and arranged in order of increasing mitotic activity corresponding to the following ranges of mitotic ratio: Grade I, M.R. 400:1 to 1,200:1; Grade II, M.R. 100:1 to 400:1; Grade III, M.R. less than 100:1. Of the 66 sarcomata, 10 fell in Grade I, 39 in Grade II, and 17 in Grade III. Study of the survival rates in this series

indicated that the 5-year rate among patients with Grade-I tumours might be " as high as 75% " and among those with Grade-II tumours 15%. Among patients with Grade-III tumours the probable 2-year survival rate was " of the order of only 12% ".

It is suggested that this type of grading may be of value in assessing prognosis and deciding treatment in these cases. *H. A. Sissons*

1084. **Regional Enteritis: Associated Visceral Changes**
L. E. CHAPIN, H. H. SCUDAMORE, A. H. BAGGENSTOSS, and J. A. BARGEN. *Gastroenterology* [*Gastroenterology*] 30, 404–415, March, 1956. 3 figs., 26 refs.

The records of a series of 39 cases of regional enteritis in which necropsy was performed at the Mayo Clinic during the period 1923 to 1954 are reviewed. The ages of the patients (27 males and 12 females) at death ranged from 14 to 65 years (average 54) and the duration of the disease from 6 months to 19 years (average 5 years).

General peritonitis was the commonest cause of death (19 cases), followed by pneumonia (5); congestive heart failure and uraemia each caused 3 deaths. Internal fistulae were found in 8 patients, external in 4, and both types in 2. The disease involved the terminal ileum in all cases; it also involved the jejunum in 5 and the stomach and duodenum in one case. In 15 instances the pathological process extended into the colon; in addition there were 2 cases with lesions in the colon resembling microscopically those of ulcerative colitis. The liver was more frequently affected than any other organ. In 20 cases there was fatty infiltration of varying intensity, while in 14 there were small foci of necrosis scattered through the lobules, the necrosis in 10 being accompanied by an acute inflammatory reaction. Leucocytic infiltration of portal spaces was observed in 4 patients. Portal cirrhosis was present in 3, only 2 of whom had a history of alcoholism. In 15 cases there was fibrosis in the pancreas, distributed in the interlobar and periductal areas, with acinar dilatation in 12. Focal cortical necrosis of the adrenal glands was found in 6 cases and thrombosis of the adrenal vessels in 3. There were few significant changes in the spleen. In the kidneys glomerulitis with endothelial proliferation was noted in 13 patients and tubular changes in 22; of the latter, 12 had proximal tubular degeneration and necrosis, 6 tubular deposits of calcium, and 4 hydropic degeneration of the proximal convoluted tubules. Pyelonephritis was found in 3 and severe amyloid infiltration in 2. Since it has been suggested that regional enteritis is a form of sarcoidosis, the heart and lungs were examined for the presence of granulomatous lesions. There was a granulomatous area in one case only; this was in the lung and was caseating.

The authors consider that the fatty lesions in the liver are similar to those associated with ulcerative colitis and are due to poor nutrition resulting from deficient diet and diarrhoea. Peritonitis did not appear to be a major cause of the focal necrosis in the liver. The glomerular lesions were not associated with any functional abnormality other than albuminuria and urinary casts. Glomerulitis and the tubular changes occur in many acute and chronic diseases and are thought to be non-specific. The hydropic degeneration of the proximal convoluted tubules, which occurred in 4 cases, has been noted in cases of ulcerative colitis; there is possibly some relationship between this lesion and chronic intestinal disease. The 2 cases of amyloidosis in such a small series suggest that this complication may be much more common than is generally believed.

The authors state in conclusion that these changes in the viscera are not specific to regional enteritis and occur in many other chronic debilitating diseases.

A. Gordon Beckett

1085. **Histogenesis of Coarse Nodular Cirrhosis**
H. F. SMETANA. *Laboratory Investigation* [*Lab. Invest.*] 5, 175–193, March–April, 1956. 18 figs., bibliography.

Because of the superficial similarity of their macro- and microscopic appearance coarse nodular cirrhosis (posthepatic, postnecrotic, toxic, or nodular cirrhosis; nodular hyperplasia of the liver) and portal (Laënnec's, alcoholic, atrophic) cirrhosis are often linked together; moreover, the two conditions produce very similar clinical pictures. But whereas in coarse nodular cirrhosis the normal liver parenchyma is replaced by " fairly uniform multilobulated nodes composed of regenerated liver cells, separated from their neighbors by a fibrous capsule ", in portal cirrhosis it is replaced by " rather uniform monolobular pseudolobules which are surrounded by fibrous septa ".

From a study of cases in the files of the U.S. Armed Forces Institute of Pathology, Washington, D.C., the author concludes that " coarse nodular cirrhosis is the result of regeneration and reorganization of liver tissue after a single but massive and severe injury, followed by uninterrupted repair " and that portal cirrhosis " represents the end stage of repair of focal injury to individual or small groups of liver cells followed by regional regeneration, regrouping, and reorganization of the hepatic columns, resulting in formation of pseudoacini which represent single units ". The pseudolobulation which is characteristic of portal cirrhosis is the result of the replacement and displacement of parts of the affected lobule by groups of regenerating liver cells, causing marked distortion of the original architecture. The nodular transformation of the liver characteristic of coarse nodular cirrhosis on the other hand is due to multicentric regeneration from surviving liver cells within an organ whose stroma and vascular elements are essentially preserved. In the author's opinion the latter condition is an occasional consequence of acute viral hepatitis, though never the result of chronic hepatitis, whereas in none of the cases of portal cirrhosis studied in which there was a history of acute viral hepatitis could the condition be attributed unequivocally to the hepatitis alone, nor was transition from chronic hepatitis to portal cirrhosis observed. Typically, portal cirrhosis followed acute focal necrosis due to alcoholic poisoning, a condition in which the argentophilic reticulum fibres often appear split and interrupted, in contrast to the lesions of viral hepatitis, which spare the reticular stroma.

E. Forrai

Microbiology and Parasitology

1086. **Is the Malaria Parasite within or upon the Red Blood Corpuscle? With Particular Reference to the Significance of Stippling and Other Morphological Changes Observed in the Host Cell**

P. G. SHUTE and M. MARYON. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 139–149, March, 1956. 5 figs., 11 refs.

Although it is generally accepted that the malaria parasite is situated inside the erythrocyte, a number of authorities have maintained that it is attached to the outer surface of the host cell. In the present paper from the M.R.C. Malaria Reference Laboratory, Horton Hospital, Epsom, the authors advance arguments in favour of the latter point of view.

They first discuss the well-known changes which are produced in the erythrocyte by the four species of *Plasmodium* found in man and the appearance of the parasites themselves. It is shown that these vary considerably according to whether thick or thin blood films from the same patient are examined. Thus band forms of *P. malariae* and oval or distorted erythrocytes infected with *P. ovale* are both common in thin films, but are rare or absent in thick films, suggesting that they should be regarded as artefacts. Stippling of the erythrocytes can be demonstrated in infections with all four species under suitable conditions, especially when the stain is first applied undiluted as in Leishman's and Wright's methods, thereby facilitating its absorption by the erythrocytes. To explain this phenomenon the authors advance the hypothesis that the malaria parasite is attached to the surface of the erythrocyte, and produces processes which puncture or otherwise damage the host cell, thereby enabling the parasite to feed on its contents. When the film is stained these perforations in the host-cell are filled with a deposit of the stain, producing the effect of stippling. When thin, moist films are examined many stippled erythrocytes are to be seen without parasites, while numerous free parasites are present, and yet the stippled cells show no sign of a rupture of their envelope due to parasites escaping from inside. The inference, therefore, is that the parasites have become detached from the surface of the cells.

Further evidence of the extracellular position of the parasites is provided by the examination of very thin films dried instantaneously, when the trophozoites of *P. falciparum* can frequently be seen to protrude beyond the outline of the host cell. Although this appearance is rarely seen in blood infected with *P. malariae*, the absence of band forms in thick films suggests that their presence in thin films may be due to the distortion of parasites lying on the cell surface by the process of spreading the film, the parasite being fixed in the distorted form owing to the instantaneous drying of the film; this explanation would also account for the fact that the elongated form of *P. ovale* seen in thin films is always stretched in the same direction as the host cell. Again, in infections with *P. vivax*, in films containing free parasites the abandoned erythrocytes show no evidence of damage to their wall. (The appearances described are illustrated in a number of plates.)

Finally, it is argued that since the effect of mepacrine on the parasite is first to cause clumping of the pigment grains and then their disappearance many hours before disintegration of the cytoplasm takes place, any extruded pigment would be retained in the erythrocyte if the parasite were intracellular, whereas in fact it appears to be released into the plasma, the possibility that it is dissolved by the mepacrine being considered most unlikely.

[The case for the intracellular position of malaria parasites is presented in the following paper (see Abstract 1087).] *C. A. Hoare*

1087. **The Relation of *Plasmodium berghei* and *Plasmodium knowlesi* to their Respective Red-cell Hosts**

J. D. FULTON and T. H. FLEWETT. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 150–156, March, 1956. 12 figs., 27 refs.

In order to determine the position occupied by malaria parasites in relation to the host cell, the authors have studied sections of erythrocytes infected with *Plasmodium berghei* and *P. knowlesi* by phase-contrast and electron microscopy. For this purpose blood from infected rats (with heparin as anticoagulant) was centrifuged and the erythrocytes re-suspended in 0·55% or 0·85% saline and fixed in 2% osmic acid, after which they were suspended in 70% alcohol, dehydrated in absolute alcohol, and embedded in a mixture of butyl- and methylmethacrylate. After solidification of the plastic, sections 2 to 10 μ and 0·25 mm. thick were cut for phase-contrast microscopy, and 0·01 to 0·05 μ thick for electron microscopy.

In plastic-embedded preparations of suspensions in 0·55% saline examined by phase-contrast microscopy the erythrocytes were globular, and by focusing up and down it could be seen that the parasites were always inside the host cells. Moreover, in preparations of suspensions in isotonic saline which were treated with xylol to dissolve away the plastic, the infected cells could be seen streaming slowly to the edges of the cover-slip as the xylol evaporated and could be observed from all sides, leaving no doubt that the parasites were intracellular. Likewise in sections examined by electron microscopy of suspensions in normal saline, in which the erythrocytes were orientated at random to the plane of section, the parasites were invariably situated inside the host cell. The authors "have photographed several hundreds of cells and inspected several thousand on the fluorescent screen of the electron microscope without ever noting any appearance to suggest that a parasite was on the surface of a cell". [The intracellular position of the

parasites is convincingly illustrated in a series of electron micrographs.] In the course of the investigation certain details of the cytological structure of the parasites were noted and are described.

[The case for the extracellular position of malaria parasites is presented in the preceding paper (see Abstract 1086).] *C. A. Hoare*

1088. **Microculture Method for the Diagnosis of Tuberculosis.** (Значение метода микрокультивирования в текущей диагностике туберкулеза)
K. V. Shmalii and G. L. Nakhmanson. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 69–70, No. 2, March–April, 1956.

The authors describe a microculture method for the diagnosis of tuberculosis, used by them at the Institute for Research in Tuberculosis, Kharkov, whereby, they claim, diagnosis can be made in 7 to 10 days. The method is as follows. Smear preparations of pathological material in which tubercle bacilli cannot be found are dried in air, treated for 6 to 8 minutes with 6% sulphuric acid, washed with distilled water for 5 minutes, and placed in test tubes containing nutrient medium, the test tubes being then sealed and kept at 38° C. for 10 days. Staining is with Ziehl–Neelsen stain. Of 200 such microcultures, 40% gave positive results. The authors recommend the method for its technical simplicity.
R. Crawford

1089. **Electron Microscopy of the Leprosy Bacillus: a Study of Submicroscopical Structure**
E. M. Brieger and A. M. Glauert. *Tubercle* [*Tubercle (Lond.)*] **37**, 195–206, June, 1956. 15 figs., 18 refs.

1090. **The Flocculation Test with a Purified Antigen in the Diagnosis of Trichinosis in Humans**
L. Norman, A. W. Donaldson, and E. H. Sadun. *Journal of Infectious Diseases* [*J. infect. Dis.*] **98**, 172–176, March–April, 1956. 9 refs.

In order to compare the results of a flocculation test with those of the standard complement-fixation test used in the serological diagnosis of trichinosis in man the authors, working at the Communicable Disease Center of the U.S. Public Health Service, Atlanta, Georgia, carried out parallel tests on 1,331 sera by both methods. An acid-soluble protein-fraction antigen prepared according to the method described by Melcher (*J. infect. Dis.*, 1943, **73**, 31) was used for the flocculation test, carried out according to the technique of Bozicevich *et al.* (*Publ. Hlth Rep.* (*Wash.*), 1951, **66**, 806). A whole-larval antigen was used for the complement-fixation test.

There was close agreement between the results of the two tests in 79% and conflicting results in 11% of the 1,331 sera examined. The remaining 10% were anticomplementary in the complement-fixation test. In 206 cases in which full clinical and other laboratory data were available the results showed close correlation between the two tests.

The flocculation test has the advantages that its result is rapidly known and is easily read, it does not require highly skilled operators, it permits the examination of sera which are anticomplementary to the complement-fixation test, and the antigen remains stable for long periods of time. Because of these considerations the authors regard the flocculation test as the test of choice for the serological diagnosis of trichinosis in man.
C. L. Pasricha

1091. **Serological Investigations on Trichomonads.** (Serologische Untersuchungen über Trichomonaden)
K. E. Schoenherr. *Zeitschrift für Immunitätsforschung und experimentelle Therapie* [*Z. ImmunForsch.*] **113**, 83–94, April, 1956. 12 refs.

At the University of Freiburg im Breisgau the serological differentiation of the various trichomonads found in animals and man was attempted by means of the precipitation reaction, complement-fixation, and agglutination of fragmented cells. Culture of *Trichomonas vaginalis* was attempted from the vaginal secretions of 83 women; good growth was obtained in 42% of specimens from 55 women who complained of discharge, as against 36% of those from 28 women who were symptom-free. The sediment of fresh cultures was repeatedly washed in physiological saline solution and then frozen and thawed 3 to 5 times in order to fragment the cells. The cell fragments were removed by centrifugation and the supernatant fluid filtered through Seitz filters, the cell fragments being used for the agglutination reaction. For the precipitation reaction rabbits were immunized with the various *Trichomonas* cultures and their immune serum used in the reaction. The trichomonads investigated were *T. vaginalis*, *T. foetus* of calves, *T. columbae* of pigeons, and *T. ardin-delteili* of hamsters.

The precipitation test and, especially, the cell-fragment agglutination test enabled the author to differentiate the various trichomonads from each other. *T. vaginalis* showed two serologically different types, but there was no serological difference between organisms recovered from symptomatic and asymptomatic women. The complement-fixation reaction was of little use since it gave largely non-specific results. The use of non-fragmented trichomonads for agglutination reactions was tried, but was found to be difficult or impossible to carry out, as the organisms grew in sheets in the culture medium; this was particularly notable in cultures of *T. vaginalis* and *T. ardin-delteili*. Fragmentation of the cells not only separated these growths into agglutinable units, but also resulted in a stronger agglutination reaction than with intact trichomonads, which appeared to have only a scanty amount of reacting antigens on their surface. *G. W. Csonka*

1092. **Effect of Added Toxoids on the Antigenicity of *H. pertussis* Vaccines**
J. Ungar. *British Medical Journal* [*Brit. med. J.*] **1**, 841–842, April 14, 1956. 10 refs.

The addition of diphtheria toxoid or of diphtheria and tetanus toxoids to a pertussis vaccine has no adverse effect on the antigenic response of mice to it. This finding indicates that combined prophylactics will induce in children the same degree of protection against whooping-cough as will a plain suspended vaccine.—[Author's summary.]

Pharmacology

1093. **N-Acetyl-*p*-aminophenol (Tylenol Elixir) as a Pediatric Antipyretic–Analgesic**
D. A. CORNELY and J. A. RITTER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1219–1221, April 7, 1956. 18 refs.

An elixir, " tylenol ", containing N-acetyl-*p*-aminophenol, the active metabolite of acetanilide and phenacetin, was administered over periods of one to 9 days at the Philadelphia General Hospital to 121 children with fever and pain due to various acute illnesses. The dosage of the drug was 60 to 240 mg. 4 to 6 times a day, according to age. Specific antibiotics and sulphonamides were given in addition to tylenol to 96 of the children, in 66 of whom the antipyretic response was good or excellent; the authors state, however, that this response could not be ascribed to any one medicament. In 18 out of 20 children [*sic*] receiving tylenol only, the antipyretic response was " good to excellent ". Altogether tylenol was considered to have given good relief of pain in 68 out of the 121 patients and moderate relief in 37.

No definite side-effects were detected in the 121 children suffering from an acute illness or in the 20 others with chronic disease (tuberculosis) to whom the drug was given for 5 weeks as a test of toxicity. In the latter group the haemoglobin level, cell morphology, leucocyte count, and the prothrombin, coagulation, and bleeding times remained normal. The drug was liked by or " acceptable " to 122 of the 141 children. [" Panadol " is a British preparation of N-acetyl-*p*-aminophenol.]

T. B. Begg

1094. **Clinical Effectiveness and Safety of a New Series of Analgesic Compounds**
A. J. GROSSMAN, M. GOLBEY, W. C. GITTINGER, and R. C. BATTERMAN. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **4**, 187–192, Feb., 1956. 2 refs.

A clinical trial of 1-methyl-4-carbethoxy-4-phenylhexamethylenimine (Wy-401), a fairly potent analgesic drug which can be given by mouth to ambulant patients suffering from moderately severe pain, is described in this paper from New York Medical College. The drug is chemically similar to pethidine, but has one ring of seven members instead of six; it possesses an analgesic potency greater than that of codeine and is much less toxic. In oral doses of 50 to 150 mg. 4 times a day it produced satisfactory relief of pain in 20 out of 29 ambulant patients. Slight nausea developed in one patient and anorexia in one. In a similar dosage it relieved severe pain in 7 out of 14 hospital patients suffering from cancer. Wy-401 did not appear to be a drug of addiction, since no withdrawal symptoms were observed in 6 patients treated for 11 to 18 weeks, and it had no effect on the withdrawal symptoms in heroin and pethidine addiction. In doses of 90 to 240 mg. intramuscularly it produced analgesia lasting 5 to 7 hours. The pain relief was considered to be satisfactory on 36 out of 57 occasions on which the drug was given. The authors recommend 180 or 240 mg. for severe pain. No significant side-effect, such as sedation, cough depression, respiratory depression, or disturbance of bowel or urinary function, was noted.

The 1:2-dimethyl and 1:5-dimethyl derivatives (Wy-682 and Wy-782) were also tested, but a total of 32 trials with each drug indicated that they were less effective as analgesics than Wy-401, although the optimum dose of each was not determined.

T. B. Begg

1095. **Acetyl-digitoxin (Acylanid): Rapid Digitalization and Maintenance by Oral Administration**
I. C. BRILL, P. R. BURGNER, and N. A. DAVID. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 707–716, April, 1956. 1 fig., 12 refs.

It has been claimed for acetyldigitoxin, a recently introduced cardiac glycoside prepared by controlled enzymatic degradation of lanatoside A, that it has a rapid onset of action, is fairly rapidly eliminated, and is relatively free from toxic effects. At the University of Oregon Medical School, Portland, the authors have tested these claims in clinical trials on two groups of patients: (1) 26 patients admitted to hospital with an acute cardiac condition requiring immediate digitalization and who had not previously received digitalis therapy; (2) 46 ambulant patients in private practice who were on maintenance treatment with a digitalis preparation, which was then replaced by acetyldigitoxin.

It was found that digitalization could be satisfactorily achieved by the administration of 0·8 mg. of acetyldigitoxin orally, followed by 0·4 mg. every 2 hours to a total dose of 1·6 mg. Some of the patients required one or two additional doses of 0·2 mg. at 4- to 6-hour intervals for complete digitalization. Maintenance therapy required the daily administration of 0·15 mg. of the drug. There was one death in the series, that of a woman of 86 who received in error 2·4 mg. of acetyldigitoxin over a period of 21 hours and who died shortly afterwards with persistent vomiting, a 2:1 heart block, and hyperkalaemia.

The authors conclude from this study that acetyldigitoxin has the following advantages: (1) it is rapidly absorbed on oral administration, has a short latent period, and acts promptly; (2) because it is more slowly dissipated than digoxin, it is more suitable for maintenance therapy; (3) it is more rapidly destroyed than digitoxin and therefore toxic symptoms, if they occur, are of shorter duration.

[It is not generally considered in Great Britain that digoxin is unsuitable for maintenance therapy.]

Bernard Isaacs

1096. **Protective Effect of Lobeline in Experimental Pulmonary Oedema.** [In English]
D. HALMÁGYI, A. KOVÁCS, P. NEUMANN, and S. KENÉZ. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **106**, 17–27, April 1, 1956. 4 figs., 19 refs.

The effect of large doses of lobeline in experimental pulmonary oedema was studied at the University Medical School, Szeged, Hungary. Lung oedema was produced in rats by bilateral vagotomy, by injection of ammonium chloride intraperitoneally or large doses of adrenaline intravenously, by α-naphthyl-thiourea, or by exposure to chloropicrin vapour. Immediately afterwards lobeline in a dosage of 20 to 100 mg. per kg. body weight was given by subcutaneous or intraperitoneal injection to test groups. The weight of the lungs in these animals (expressed as a percentage of the body weight) either at the time of death or at a predetermined time interval after oedema was induced was compared with that of animals not receiving lobeline. Administration of large doses of lobeline to otherwise untreated rats caused restlessness, convulsions, and death in 15 to 25 minutes. Restlessness and convulsions were not observed, however, if the animals were previously given " narconumal ". The lungs were also examined histologically, and from the findings it was concluded that lobeline in toxic doses was effective in preventing lung oedema produced by any of the procedures described above. Other respiratory stimulants, antihistaminics, ganglion-blocking agents, and central nervous system depressants were ineffective in preventing the lung oedema. The mechanism whereby lobeline exerts its effect is unknown. *P. A. Nasmyth*

1097. **Depression of Gastric Secretion by a New Anticholinergic Agent**
A. P. KLOTZ. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **1**, 108–115, March, 1956. 2 figs., 4 refs.

This paper from the University of Kansas Medical Center, Kansas City, reports a study of the pharmacology of a 3-hydroxypiperidine derivative, N-ethyl-3-piperidyl-benzilate methobromide (" piptal "), with special reference to its effect on gastric secretion in man. This compound is an anticholinergic agent and is rapidly absorbed from the gastro-intestinal tract of animals, the duration of its effect being 2 to 3 hours. Acetylcholine-induced vasodepression is partially inhibited within 5 minutes and completely blocked within 10 to 15 minutes of the injection of 0·5 mg. per kg. body weight into the dog's stomach. This effect is similar to that of atropine, but lasts longer.

Short-term studies of the effect of piptal on gastric secretion were carried out on 88 patients, in most of whom gastric secretion was known to be excessive. A Levin tube was passed and the fasting secretion removed, followed by 4 samples of gastric juice at 15-minute intervals. The drug was then instilled through the tube and after one hour samples were again collected at 15-minute intervals for 2 hours. The dose varied from 5 to 20 mg. In 77 cases there was a decrease in the gastric output of free acid, which fell to one-half of the basal level or below in 60, while in 35 cases (40%) anacidity was produced for 30 minutes or longer. The response of different patients to the same dose, and of the same patient to different doses, varied considerably, a larger dose sometimes having less effect than a small dose.

A second series of 20 patients with duodenal or pyloric ulcer under medical treatment received 5 mg. of piptal 4 times daily over " a number of months ", periodic gastric analyses being performed to see whether prolonged administration had any lasting effect on the basal secretion. Only in a few cases was the basal secretion decreased after 3 months' treatment, and in some cases the values were higher at the end of that period than at the beginning. No marked side-effects were observed —a unique finding in a potent antisecretory drug.

The author concludes that the anticholinergic drugs at present available serve as a supplement to, but not a substitute for, antacid therapy in the treatment of peptic ulcer, and that piptal marks a desirable advance in the development of highly potent antisecretory agents with a minimum of side-effects. *E. Forrai*

1098. **Effect of a Phenylbutazone Analog (4-[Phenylthioethyl]-1:2-diphenyl-3:5-pyrazolidinedione) on Urate Clearance and Other Discrete Renal Functions in Gouty Subjects. Evaluation as Uricosuric Agent**
T. F. YÜ, B. C. PATON, T. CHENKIN, J. J. BURNS, B. B. BRODIE, and A. B. GUTMAN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 374–385, April, 1956. 2 figs., 15 refs.

As part of an investigation of various derivatives of phenylbutazone, undertaken in an attempt to discover an analogue with the antirheumatic properties but without the undesirable side-effects of the parent compound, the effect of one of these, G-25671, was compared with that of phenylbutazone on the renal clearances of inulin, PAH, urate, sodium, potassium, and chloride in 12 gouty male patients aged 33 to 62 at the Mount Sinai Hospital, New York. Both drugs depressed the clearance of PAH, apparently as a result of decreased renal extraction. Inulin clearance was not usually affected, although it was reduced in some instances. G-25671 had a much more pronounced uricosuric action than phenylbutazone, probably owing to suppression of tubular reabsorption of urates, and it caused distinctly less sodium and chloride retention. The excretion of potassium and phosphate was unaffected.

In a clinical trial on 28 gouty patients who received doses of 1 to 2 g. of G-25671 daily, the mean serum uric acid level was reduced from 9·6 mg. to 4·7 mg. per 100 ml. The effect on patients with renal damage was less satisfactory. The drug controlled the pain and stiffness of chronic gouty arthritis, but in this respect was less effective than phenylbutazone. It was of little or no value in terminating acute gouty attacks. A drug rash developed in 3 (10%) of the patients. There was no evidence of bone-marrow depression or of toxic effects on the liver or nervous system but, as the authors admit, the observations were too few and the study too brief to warrant any definite conclusions. *Norval Taylor*

Chemotherapy

1099. **Studies on Novobiocin, a New Antimicrobial Agent**
H. J. SIMON, R. M. MCCUNE, P. A. P. DINEEN, and D. E. ROGERS. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 205–218, April, 1956. 7 figs., 2 refs.

Novobiocin (streptonivicin; " albamycin ") is a new antibiotic isolated from cultures of the actinomycete *Streptomyces niveus*. Like penicillin it is an acid substance and is freely soluble in water at room temperature as the monosodium salt. In a study carried out at New York Hospital–Cornell Medical Center, New York, the susceptibility to novobiocin of seven micro-organisms was assessed *in vitro* by the tube dilution method, and its effectiveness against staphylococcal and *Proteus* infections in mice and its absorption and distribution in man were also investigated.

The results of this limited trial showed that novobiocin is relatively non-toxic and possesses significant activity *in vitro* against most strains of *Staphylococcus aureus*, pneumococci, and Group-A streptococci. Gram-negative organisms, however, proved resistant, except for several strains of *Proteus* which were moderately sensitive. Experimental *Proteus* and staphylococcal infections in mice responded to treatment with the new antibiotic. In man novobiocin was shown to be rapidly absorbed following ingestion, peak serum concentrations occurring in 2 hours when it was taken in the fasting state or in 4 hours if taken after a meal. A high degree of protein-binding, principally affecting the serum albumin, was observed, but the linkage was presumably a loose one, since high urinary concentrations of the drug appeared within 8 hours of absorption. Novobiocin was found to diffuse into the pleural and peritoneal cavities, but was not detected in the cerebrospinal fluid.

D. Geraint James

1100. **Clinical Effectiveness and Safety of Novobiocin**
N. A. DAVID and P. R. BURGNER. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 219–229, April, 1956. 12 refs.

Before reporting the results of a clinical trial of novobiocin the authors first clear up some confusion regarding the name of this new antibiotic obtained from *Streptomyces niveus*. It was first announced in November, 1955, under the generic name of streptonivicin and has since been given the proprietary names of " cathomycin " and " albamycin ", but the latter should not be confused with the antibiotic " albomycin " reported from the U.S.S.R. by Gause (*Brit. med. J.*, 1955, **2**, 1177; *Abstracts of World Medicine*, 1956, **20**, 11), with which it is apparently not identical.

The authors have observed the effects of novobiocin in the treatment of a variety of infections in 29 patients at various hospitals in Portland, Oregon. It was found to be particularly useful in staphylococcal infections, even in cases in which other antibiotics had previously failed. Its toxic effects were mild and few; they included rashes, neutropenia, eosinophilia, gastro-intestinal disturbances, and an increased icteric index, which is thought to be due to a yellow pigment, a metabolite of novobiocin, in the plasma.

D. Geraint James

1101. **Novobiocin: a Laboratory Investigation**
G. LUBASH, J. VAN DER MEULEN, C. BERNTSEN, and R. TOMPSETT. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 233–240, April, 1956. 2 figs., 1 ref.

A preliminary laboratory investigation of the properties of novobiocin at the Bellevue Hospital, New York, revealed that it is effective against Gram-positive cocci in a concentration of 0·4 μg. per ml. of liquid medium, but ineffective against Gram-negative organisms except certain *Proteus* strains, which exhibited moderate sensitivity. Of the 48 strains of *Staphylococcus aureus* tested, 43 were resistant to streptomycin, 40 to penicillin, 20 to tetracycline, 9 to chloramphenicol, and 5 to erythromycin; thus there was no evidence of cross-resistance between novobiocin and the commonly used antibiotics. The activity of novobiocin *in vitro* was markedly inhibited by the presence of serum, probably because of its high binding capacity with serum albumin, and the authors suggest this may turn out to be a serious drawback to the clinical use of the drug. In a small test on human subjects novobiocin was shown to be well absorbed when administered orally, ingestion being followed by high blood concentrations; it was not demonstrable in either cerebrospinal or pleural fluid, but was present in the bile. Side-effects in the form of a skin eruption occurred in 2 out of 30 subjects.

D. Geraint James

1102. **Novobiocin: a Limited Bacteriologic and Clinical Study of Its Use in Forty-five Patients**
R. L. NICHOLS and M. FINLAND. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 241–257, April, 1956. 18 refs.

The bacteriological and clinical effects of novobiocin administered orally have been observed at the Boston City Hospital in 45 patients, most of whom had either staphylococcal infections or various infections of the urinary tract. The most frequent dosage schedule employed was 500 mg. every 6 hours for periods of 2 to 30 days (average 9·6 days). The drug was well tolerated and the only toxic effects were rashes and fever in 4 cases. Studies *in vitro* had shown that most strains of *Staphylococcus aureus* were sensitive to the drug, but during the course of treatment increasing resistance to novobiocin was liable to develop. Nevertheless the clinical results were satisfactory in most, but not all, of the staphylococcal infections. Many strains of *Proteus* were inhibited *in vitro* by relatively small concentrations of the antibiotic, whereas others were resistant. Both *Proteus* and *Staph. aureus* appeared to be more sensitive when the *p*H of the liquid medium was decreased from 8·1 to 5·5. For

his reason patients with urinary-tract infections due to *Proteus* organisms were also given oral ammonium chloride to maintain an acid urine. In these infections, however, both the bacteriological and the clinical results were disappointing, for except in one case the course was not appreciably affected. Similarly, in urinary infections due to coliform organisms the results were equivocal. It is concluded that the effect of novobiocin in combination with other antimicrobial agents in the treatment of staphylococcal infections deserves further investigation. *D. Geraint James*

1103. **Novobiocin: Further Observations**
W. J. MARTIN, F. R. HEILMAN, D. R. NICHOLS, W. E. VELLMAN, and J. E. GERACI. *Antibiotic Medicine [Antibiot. Med.]* **2**, 258–267, April, 1956. 7 refs.

This report from the Mayo Clinic outlines the authors' clinical experience with novobiocin in the treatment of 74 patients with various infections, and also indicates the distribution of the drug in various tissues. Novobiocin was given by mouth in a dosage of 500 mg. (2 capsules) 6-hourly for adults or 100 mg. 6-hourly for infants. It was also administered intravenously in doses of 500 mg. every 12 hours or 250 mg. intramuscularly every 8 hours without ill effects. Rashes commonly followed its oral administration. Staphylococcal enterocolitis did not develop following its use, and it is suggested that this complication is unlikely because the Gram-negative faecal flora are unaffected by novobiocin. Successful results were obtained in the treatment of 4 out of 5 patients with staphylococcal septicaemia, 5 patients with staphylococcal enterocolitis, 3 with osteomyelitis, and one patient with a staphylococcal subphrenic abscess. *D. Geraint James*

1104. **Antibacterial Activity of Streptonivicin and Cathomycin, Two New Antibiotics**
W. F. JONES, R. L. NICHOLS, and M. FINLAND. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 47, 783–792, May, 1956. 1 fig., 2 refs.

1105. **Observations on Clinical Use of Phenoxymethyl Penicillin (Penicillin V)**
W. J. MARTIN, D. R. NICHOLS, and F. R. HEILMAN. *Journal of the American Medical Association [J. Amer. med. Ass.]* **160**, 928–931, March 17, 1956. 1 fig., 3 refs.

Phenoxymethylpenicillin has been found to be effective when given by mouth. Unlike benzylpenicillin, which is also administered orally, it is a stable acid and is not destroyed by the acids in the gastric juice. It is as active *in vitro* as other forms of penicillin, and a blood concentration adequate for bacterial inhibition is obtained with an initial dose of 400,000 units followed by 200,000 units 4-hourly. The serum concentrations 2 hours after ingestion of phenoxymethylpenicillin and of benzylpenicillin showed wide variations, but those of the former were, on the average, twice as high as those of benzylpenicillin. In cases of severe infection the dosage of phenoxymethylpenicillin should be 800,000 units 4-hourly; minor infections respond favourably to 200,000 units 4-hourly.

Phenoxymethylpenicillin was tried at the Mayo Clinic on 18 patients suffering from various infections. Aphthous stomatitis developed in one, but there were no other complications. *J. Robertson Sinton*

1106. **The Action of Six Antibiotics Singly and in Combination on Enterococci Isolated from Cases of Subacute Bacterial Endocarditis**
T. R. E. PILKINGTON, S. D. ELEK, and P. JEWELL. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* **47**, 562–572, April, 1956. 4 figs., 33 refs.

The bactericidal and bacteriostatic concentrations of 7 antibiotics, penicillin, streptomycin, erythromycin, bacitracin, chloramphenicol, aureomycin (chlortetracycline), and oxytetracycline, were measured *in vitro* by Elek and Hilson's method (*J. clin. Path.*, 1954, **7**, 37) against 18 strains of enterococci isolated from cases of penicillin-resistant subacute bacterial endocarditis; the antibiotics were tested separately and in pairs. The bactericidal concentrations *in vitro* of penicillin and streptomycin were of the same order as the bacteriostatic; the bactericidal levels of the other antibiotics, however, were much higher than the bacteriostatic. At blood concentrations which can be obtained clinically penicillin and streptomycin are predominantly bactericidal, while aureomycin, oxytetracycline, and chloramphenicol are bacteriostatic; this distinction was not demonstrated by routine laboratory tests. Of the 21 possible combinations of the drugs in pairs, synergism occurred most frequently with penicillin and streptomycin, streptomycin and bacitracin, and streptomycin and chloramphenicol; antagonism was most consistently observed between penicillin and chloramphenicol. *J. E. Page*

1107. **Protective Action of Pantothenic Acid against Toxic Effects of Streptomycin and Dihydrostreptomycin**
R. DUCROT, O. LEAU, and C. COSAR. *Antibiotics and Chemotherapy [Antibiot. and Chemother.]* **6**, 404–410, June, 1956. 2 figs., 10 refs.

The LD_{50} of streptomycin sulphate, given subcutaneously, in mice was 0·7 g. per kg. body weight and that of dihydrostreptomycin 1·2 g. per kg. The corresponding values for the pantothenates of the two antibiotics were 1·4 g. and 2·4 g. per kg. respectively.

Rats conditioned to respond to a bell were given one or other antibiotic as the sulphate in doses of 100 mg. per kg. subcutaneously daily for 15 weeks; 20 mg. of sodium pantothenate per kg. was given in addition to some of the animals, while others received 20% of the dose of antibiotic as the pantothenate and 80% as the sulphate. It was found that the onset of deafness was markedly deferred in those receiving pantothenate, whether combined with the antibiotic or separately, and any impairment of hearing was much less severe.

Administration to cats of 200 mg. of streptomycin sulphate per kg. daily for 18 days caused serious vestibular impairment, with clonic convulsions and nystagmus. Other cats given the same dose with the addition of 40 mg. of sodium pantothenate per kg. were almost completely free from disturbances of equilibrium and were able to jump and land normally. *V. J. Woolley*

Infectious Diseases

1108. **The Use of Human Serum Gamma Globulins in the Prophylaxis of Measles.** (Utilisation des gamma-globulines plasmatiques humaines dans la prophylaxie de la rougeole)
R. DEBRÉ, J. P. SOULIER, F. HERZOG, M. BADILLET, and M. GAIFFE. *Presse médicale* [*Presse méd.*] **64**, 667–669, April 11, 1956. 1 fig., bibliography.

The authors report, from the Hôpital des Enfants Malades, Paris, the results of the use of gamma globulin in the prophylaxis of measles in 1,259 children who had been exposed to the infection. The dose was 0·2 ml. of human gamma globulin per kg. body weight, subject to a maximum dose of 5 ml. and a minimum of 2 ml. Out of 1,181 cases in which sufficient information was available, in 1,062 (90%) no measles developed. In 96 cases (8%) an attenuated form of the disease appeared after an incubation period exceeding 20 days or more; it was sometimes difficult to determine the exact day of infection, but it seemed likely that in these cases the injection was given at least one week after first exposure. In 23 cases (2%) there was no apparent effect on the disease; in this last group at least three factors were considered to have contributed to the failure: (1) poor general condition of the subjects, particularly young infants; (2) repeated or persisting exposure to infection for at least 2 weeks after injection; and (3) the concurrence of another infectious disease.

Gamma globulin was also used therapeutically in the treatment of 12 cases of measles. In 8 of these no effect could be observed, but in 4 there was a subsidence of the disease within 12 hours of the injection. In all cases the gamma globulin employed was prepared at the French National Blood Transfusion Centre from human plasma and was given by intramuscular injection. Febrile reactions were commonly caused by some of the earlier batches, but these were later eliminated by more careful filtration in the process of preparation.

T. A. A. Hunter

1109. **Epidemic Hepatitis in Hot Climatic Conditions.** (К клинике эпидемического гепатита в условиях жаркого климата)
M. B. KACHUR. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 65–68, No. 4, April, 1956. 3 refs.

The author reports his observations in 400 cases of infective hepatitis ("epidemic hepatitis") admitted to hospital during the first week of the icteric stage, 89·6% of the patients being admitted within 3 days of the first change in the colour of the sclerae or of the urine. The average time of onset of this stage was on the 5th day of clinical illness. Clinical jaundice was absent in 1·7% of cases. The pre-icteric stage was marked in 99% of cases. The prevalence of various symptoms during this period was as follows: anorexia in 73·7%, lassitude in 71·2%, epigastric pain in 54·5%, right hypogastric pain in 28·4%, headache in 24%, a subjective sensation of heat in 12·2%, nausea in 9·7%, and vomiting in 5·5%. The onset was gradual in 92% of patients. The disease was manifested in a mild form in 61%, was of medium severity in 32·4%, was severe in 4·6%, and very severe, with hepatic coma, in 2%. In 75·4% of the mild cases the serum bilirubin level did not exceed 25·6 mg. per 100 ml., but in 3·7%, that is, the severest cases, this value varied from 102 to 204·8 mg. per 100 ml. A significant association of epidemic hepatitis with parasitic infestation of the gut was observed; thus *Giardia lamblia* was found in 18% of patients and helminths in 11·7%.

Treatment was based on the parenteral administration of glucose (except in the mildest cases (9%)) and of crude liver extract ("campolon"). In cases of hepatic coma 6 or 7 litres a day of 5% solution of glucose was administered intravenously. Clinical cure was recorded in 99·5% of cases.

A. Swan

1110. **Cardiorespiratory Problems in Severe Poliomyelitis Observed during the Recent Epidemic**
F. K. AUSTEN, J. KOCH-WESER, and R. A. FIELD. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 790–793, April 26, 1956. 2 figs., 4 refs.

When death in acute poliomyelitis is not due to obvious airway obstruction, ventilatory insufficiency, or some other specific complication it is generally attributed to circulatory collapse secondary to involvement of the medullary vasomotor centre or, less frequently, to circulatory collapse from myocarditis. During an epidemic of poliomyelitis in 1955, 74 out of 400 patients admitted to the Massachusetts General Hospital, Boston, had to be transferred to a respirator, and 17 of these died. Analysis of these 17 cases showed that in 6 death was due to identifiable causes other than acute poliomyelitis and in the remaining 11 to circulatory collapse. These 11 cases were divided into two groups according to the treatment administered. In the first group of 7 patients no oxygen therapy had been given and 6 of the patients had died within 36 hours of entering the respirator. The onset of circulatory collapse had been characterized by anxiety, apprehension, a dusky, florid appearance, and tachycardia, with normal blood pressure or hypertension. The patients became confused, cold, clammy, and cyanosed, and developed hypotension not responding to noradrenaline or plasma-volume expanders. All the patients were being adequately ventilated, but the electrocardiogram, obtained in 3 cases, showed changes compatible with myocardial hypoxia. At necropsy the weight of the lungs was increased and pulmonary oedema and congestion were present, but no cardiac abnormalities were found except a slight myocarditis in one case. In the second group of 4 patients oxygen therapy had been given because arterial oxygen saturation was diminished to a marked degree in the normotensive phase, and with the onset of hypotension it

was diminished still further; this persisted in spite of restoration of the blood pressure and optimal tidal exchange. Three of the patients were transferred to a Jefferson positive-pressure ventilator and carried through a period of diminished arterial oxygen saturation with supplementary intratracheal oxygen. The weight of the lungs in these cases was increased primarily as a result of bronchopneumonia and not of pulmonary oedema or congestion. These 4 patients died 1 to 4 weeks after the onset.

It is suggested that supplementary oxygen by the positive-pressure ventilator technique probably contributed materially to the survival of at least 7 other patients. The findings indicate that circulatory collapse in acute poliomyelitis is the result of pulmonary oedema and progressive " arterial oxygen unsaturation ".

A. Ackroyd

1111. **Influence of Creatine Precursors and High Energy Phosphates on Convalescence from Poliomyelitis**

A. C. Jones. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **35**, 70–83, April, 1956. 7 figs.

The author suggests that the administration of creatine precursors and the resulting availability of high-energy phosphates would be of value in hastening recovery from poliomyelitis. The loss of muscle substance which follows degeneration of the affected motor-nerve fibres and end-plates in this disease is accompanied by the excretion of large quantities of the products of muscle disintegration, particularly of phosphocreatine and adenosine triphosphate (ATP), in quantities roughly proportional to the loss of muscle substance. Further, an adequate supply of amino-acids is required for the repair of damaged tissue and recovery of nerve cells and muscle fibres which have not been irreversibly damaged. Glycocyamine (guanidoacetic acid) and betaine (trimethyl glycine) are precursors of creatine, and published reports suggest that the main reservoir of immediately available energy in muscle, creatine phosphate, can be increased by the administration of glycocyamine. ATP is essential also for the phosphorylation of sugars, the oxidation of fatty acids (subsequently converted to co-enzyme A), and the synthesis of acetylcholine.

The author has therefore studied the effect of these substances on the progress of 86 patients, ranging in age between 2 and 45 years, who were all in the stage of recovery 2 to 9 months after the onset of poliomyelitis. (A preliminary period of 2 months was allowed to elapse after the febrile illness in order to avoid the early, rapid changes in muscle strength which follow the subsidence of the acute inflammation of the central nervous system.) Manual testing by means of the standard Lovett grading technique was used, the results of this assessment being further checked by the progressive resistance–weight method described by DeLorme and Watkins. After muscle-strength curves had been established by these means medication was begun with betaine anhydride in doses of 3·5 g. and a betaine–glycocyamine compound (" betasyamine ") in doses of 0·8 g., both four times a day, so that the average total dose for an adult in 24 hours was 14·86 g. of betaine and 3·2 g. of glycocyamine, with appropriate adjustments for children. Placebo tablets of similar appearance were given [for unspecified periods] on the " double blind " principle. Initial gains in muscle strength and a euphoric response were noted during the periods of administration of the drugs, while weight increased and endurance improved in all cases. There was no apparent correlation between the ingestion of the drugs and complaints of pain in the muscles. The author concludes that the dynamic stimuli of movement are necessary for the most effective use of creatine precursors, which, however, are considered to serve a useful purpose as adjuvant therapy.

D. Preiskel

1112. **A Study of Hemolytic Streptococcal Infections in Relation to Antistreptolysin O Titer Changes in Orphanage Children**

H. Packer, M. B. Arnoult, and D. H. Sprunt. *Journal of Pediatrics* [*J. Pediat.*] **48**, 545–562, May, 1956. 24 refs.

Observations are reported on a one-year orphanage study of hemolytic streptococcal infections, during which weekly throat cultures and monthly antistreptolysin O determinations were made. When these data were analyzed in relation to clinical and subclinical illness in the study group and the influence of limited specific therapy, the following observations were made.

The high prevalence of infection with hemolytic streptococci during the early months of the study was considered to represent a convalescent carrier state, due to the low prevalence of clinical illness and the downward trend of antistreptolysin O titers. During this early period, widespread infection with Group C hemolytic streptococci was encountered, without associated clinical illness or significant increases in antistreptolysin O titer. However, the latter occurred during the subsequent months of the study in 9 children following infection with this organism.

Clinical illness and significant increases in antistreptolysin O titer were noted most frequently in the youngest age group and less frequently in the older age groups of the study, following the acquisition of Group A hemolytic streptococci. Significant increases in antistreptolysin O titer were preceded most frequently by upper respiratory illness in the youngest age group and less frequently in the older age groups, in whom subclinical infections were more common.

Nontypable Group A hemolytic streptococci encountered during our study appeared to be as capable of producing clinical illness and immunologic responses as typable organisms. Failure of prophylactic penicillin producing adequate blood levels (0·03 to 0·125 unit per ml.) to eradicate Group C hemolytic streptococci was observed in a few instances. While tetracycline hydrochloride achieved the eradication of these organisms, its administration was followed by the emergence of large numbers of staphylococci. The latter produced no adverse effects even during an epidemic of measles. The failure of short courses of penicillin and tetracycline antibiotics to eradicate hemolytic streptococci was repeatedly observed, and the implications of this in the prevention of rheumatic fever are discussed.—[From the authors' summary.]

Tuberculosis

1113. **The Recognition of Primary Tuberculous Infection of the Mouth**

J. Boyes, J. D. T. Jones, and F. J. W. Miller. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 81–86, April, 1956. 10 figs., 6 refs.

Primary tuberculous infection of the mouth is not so common as the relative frequency of submandibular tuberculous lymphadenitis would suggest. Failure to search for or recognize lesions in the mouth may account for this disparity. At the Sutherland Dental School (University of Durham) 7 patients, aged 2 to 17 years, with submandibular tuberculous lymphadenitis of recent origin were found to have painless oral ulcers and a positive tuberculin reaction. In 4 of the cases the condition followed dental extraction. In 2 the affected nodes were excised, and in 4 incision was undertaken after fluctuation had developed. Calcification in the nodes was subsequently detected radiologically in 5 cases.

The case histories are given in detail and the characteristics of the ulcers are described and illustrated. Where a tooth had been extracted the ulcer was at the site of the tooth socket or in the gingivo-labial sulcus in relation to the socket, but even in the absence of trauma the gums were the site of ulceration. Since these ulcers may heal without a scar the origin of infection in the lymph nodes may not be determined unless it is looked for early. Because of the liability to further caseation in neighbouring nodes if the node affected is allowed to soften, excision before fluctuation develops is recommended as the treatment of choice.

Wilfrid Gaisford

1114. **Sources of Tuberculous Infection in an Area Containing Bovine Tuberculosis**

D. F. van Zwanenberg, C. J. Stewart, K. M. Harding, and S. T. G. Gray. *British Medical Journal* [*Brit. med. J.*] **1**, 1464–1466, June 23, 1956. 1 fig., 16 refs.

The difficulties encountered in tracing the source of infection of tuberculin-positive children, especially in an area where milk-borne bovine tuberculosis is suspected, are well known. In a small market town in Britain (population 7,400) 5 cases of tuberculous cervical lymph nodes and one case of tuberculous peritonitis were found over a period of 4 months in 1954. The patients were children who had had milk from one particular dairy, although all four dairies in the town were distributing milk which had been satisfactory bacteriologically for a number of years. A tuberculin survey among the school-children was therefore carried out, 1,063 out of 1,360 being tested by the Heaf multiple-puncture technique. The 219 families of the 260 tuberculin-positive children were interviewed and 416 adults, with the tuberculin-positive children, were subjected to *x*-ray examination. No case of active pulmonary tuberculosis was found.

Of the 260 children, 37 had a history of definite contact with a known case of tuberculosis and a further 25 had drunk raw milk direct from a farm outside the town. The remaining 198 were grouped according to age and the dairy supplying their milk. It was found that 31 out of the 40 children aged 7 or under had milk from dairy "A". The quantities of milk supplied by the 4 dairies differed considerably, and when the numbers of tuberculin-positive children for each 120 gallons of milk supplied daily were calculated it was found that the figure for dairy "A" was 86, for dairy "B" 48, for dairy "C" 11·3, and for dairy "D" 11·3.

Inquiry showed that at dairy "A" the retailer was supplying milk from his own herd of 24 cows which in 1954 was found to contain 19 reactors to the intradermal tuberculin test. Dairy "B" had sold T.T. milk only for 4 years, but before that had sold undesignated milk. Dairy "C" had sold only pasteurized milk for the past 19 years, and dairy "D" for the past 4½ years, the latter having previously sold T.T. and undesignated milk.

Although there was no proof, it seemed likely that milk was the source of infection of the tuberculin-positive children. During the survey a further 12 cases, previously unknown, of tuberculous cervical lymph nodes were found, milk from dairy "A" being supplied in 11 cases and milk from dairy "B" in one case.

Kenneth Marsh

1115. **Effects of Isonicotinic Acid Hydrazides on Mental Status of Tuberculous Patients**

A. Zitrin and D. S. Thompson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 204–210, May 19, 1956. 18 refs.

The nature and incidence of psychoses occurring in tuberculous patients during treatment with isoniazid or iproniazid were studied with reference to 79 patients admitted to Bellevue Psychiatric Hospital, New York, between January, 1952, and March, 1954. The ages of the patients, 44 of whom were males, ranged from 13 to 81 years. Before admission treatment with isoniazid or iproniazid had been given for periods varying from less than 2 weeks to over one year, and the dosage of the drugs had ranged from 150 to 400 mg. daily. A group of 77 tuberculous psychiatric patients who had not received either drug served for purposes of comparison. There was no difference between the two groups in the first and final diagnoses. Selected case-histories show that psychotic episodes occurred when the patient was not receiving isoniazid as well as during administration of the drug. No evidence was obtained that iproniazid, which was given to 6 of the patients, precipitated the psychosis.

In a further study the incidence of psychoses in 1950 in 19,059 tuberculous patients was compared with that in 1953, after the introduction of *iso*nicotinic acid

hydrazides, in 18,261 similar patients; no significant difference between the two series was observed.

The authors consider that the incidence of psychosis due to isoniazid therapy, if indeed such cases occur at all, must be very low, and that a history of mental disorder or of suspected toxic mental reaction to isoniazid is not a contraindication to the use of this drug.

G. de M. Rudolf

DIAGNOSIS AND PROPHYLAXIS

1116. **The Heaf Multiple Puncture Test Compared with the Mantoux Test in Epidemiological Surveys**

E. M. RATHUS. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 696–698, April 28, 1956. 1 fig., 3 refs.

A comparative study of the reliability and accuracy in tuberculosis surveys of the Heaf multiple-puncture test and the Mantoux test is reported from the Brisbane Chest Clinic, the former test being performed in accordance with Heaf's original description (*Lancet*, 1951, **2**, 151) and the latter consisting in intradermal injection of 10 units of old tuberculin. The site for both tests was the flexor surface of the forearm. Altogether 1,052 subjects given B.C.G. vaccine and 2,944 unvaccinated subjects were tested, 95% being under 19 years of age. Among the unvaccinated subjects the percentage of positive results was slightly higher with the Heaf test than with the Mantoux test (26·8% compared with 25·3%), but in the vaccinated subjects the percentages were substantially the same (90·5 and 90·4% respectively). There were a number of discrepancies in the results among the weakly-positive reactors, some who gave a negative reaction to the Mantoux test being positive reactors to the Heaf test and vice versa. There was good correlation among subjects giving more strongly positive reactions.

The ease with which the Heaf test can be carried out under epidemiological conditions is confirmed. It is concluded that this test is just as reliable as the standard Mantoux test.

John M. Talbot

1117. **Methods and Results of Antituberculosis Vaccination in Czechoslovakia.** (Методы и результаты предохранительной вакцинации против туберкулеза в Чехословакии)

L. SHULA. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 13–20, No. 2, March–April, 1956. 9 refs.

In Czechoslovakia B.C.G. vaccination is compulsory for all persons up to 30 years of age who give negative tuberculin or B.C.G. reactions. Details of the strains used and of the methods of preparation of the vaccines are given. The following figures are quoted to show the effectiveness of B.C.G. vaccination. In the period 1950–3, of 520 children with bacteriologically-positive tuberculosis, 12 had been vaccinated and 485 were unvaccinated, while in the nine months January to September, 1954, there were 67 cases of tuberculosis, 5 in vaccinated children and 60 in unvaccinated.

Full information regarding the effectiveness of the mouse vaccine is not yet available, but of 16,335 persons given B.C.G. vaccination in 1952, one developed tuberculosis in the year of vaccination, and among 4,654 persons vaccinated with the mouse strain, no case developed in the same year. In 1953, when 10,544 B.C.G. and 11,354 mouse-strain vaccinations were performed, one case of tuberculosis developed in each group. A rise in the ratio of vaccinated to unvaccinated subjects with the lapse of time indicates that the procedure has its greatest effectiveness in the first year after vaccination; these ratios were as follows: 1950, 1:35; 1951, 1:25; and 1952, 1:11. Revaccination is prescribed after 5 years. Writing from the Tuberculosis Research Institute, Prague, the author states that the mouse-strain vaccine is to be used increasingly in the future since its original low virulence is thought to obviate any possibility of enhancement of virulence, such as might occur with the originally virulent Calmette–Guérin strain.

R. Crawford

EXTRA-RESPIRATORY TUBERCULOSIS

1118. **Tuberculous Polyserositis**

R. M. ACHESON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 159–174, April, 1956. 7 figs., bibliography.

The literature on tuberculous polyserositis is reviewed and a case treated at the Radcliffe Infirmary, Oxford, is described.

An 11-year-old girl with grossly enlarged mediastinal lymph nodes developed effusions into all 4 serous sacs. She was intensely sensitive to 1 in 100,000 old tuberculin, and tuberculous polyserositis was diagnosed, this diagnosis being later confirmed by isolation of *Mycobacterium tuberculosis* from the pleural fluid. After a phase of cardiac failure the pericardial and pleural effusions resolved, but ascites persisted and required frequent tapping. When the patient's condition was reassessed 2 years later there was evidence of recent miliary spread and active foci were found in the right lung, both kidneys, and the second lumbar vertebra. Streptomycin and tuberculin were administered for 9 consecutive months, with improvement. Two years later still the full syndrome of constrictive pericarditis was present and pericardectomy was performed. During the following year the ascites and oedema disappeared, but a left nephrectomy was necessary because of residual active disease. Three months after this operation severe biliary colic necessitated removal of the gall-bladder. The patient has led a full and healthy life for the last 4 years.

In the total of 42 cases (41 reported in the literature) the sex incidence and age distribution of the syndrome appeared to be similar to those of primary tuberculous serous effusion, the condition being commonly seen in patients between 15 and 24 years of age. Ten of the patients died from miliary tuberculosis within 4 years and 13 from heart failure due to constrictive pericarditis within 9 years of the onset.

The author considers that in the early stage of the disease the multiple effusions are caused by an active tuberculous process in a hypersensitive individual with extensive lymphatic involvement. The ascites and heart

failure in the later stages are due to fibrosis and hyalinization of the serous membranes following the initial inflammation. To prevent fibrosis of the serous membranes prolonged administration of streptomycin and isoniazid with concomitant adrenal corticosteroid therapy is advised, pericardectomy being performed if this treatment fails. *I. Ansell*

RESPIRATORY TUBERCULOSIS

1119. **The "Quiescent" Tuberculous Bronchus. A Review with a Study of Its Surgical Connotations**
K. L. HARDY and P. C. SAMSON. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 73, 451–471, April, 1956. 11 figs., 41 refs.

The history of the management of cases of bronchial tuberculosis is reviewed, from pre-chemotherapeutic days, when this complication was regarded as serious, through the early chemotherapeutic period, when it was regarded with complacency, to the recent renewal of concern about the increasing incidence of bronchopleural fistulae after resection—7% in a recently published series of cases. The authors claim that the presence of mucosal tuberculous infection can be diagnosed bronchoscopically, and that when the mucosa appears normal or pale the tuberculous bronchus can be regarded as "quiescent" and resection is then safe. At Highland–Alameda County Hospital, Oakland, California, resection was performed in 105 consecutive cases of pulmonary tuberculosis in which the bronchus appeared to be quiescent as a result of chemotherapy; in none of these did bronchopleural fistulae develop after operation. Histological examination of the resected bronchi confirmed mucosal healing but often revealed submucosal tuberculosis; for this reason the term quiescent is preferred to healed. It is stated that in most cases bronchial tuberculosis will become quiescent in response to chemotherapy, but other measures which may be employed to reduce the amount of infectious sputum traversing the bronchus include thoracoplasty, Monaldi drainage, and cavernostomy. Drainage may also be encouraged by the use of aerosols of detergents and bronchodilators.
C. M. Fletcher

1120. **The Treatment of Pulmonary Tuberculosis with ACTH and Bacteriostatics.** (La terapia ACTH–batteriostatica della tubercolosi polmonare)
M. REALE, A. GARAVENTA, G. PAOLI, and G. COSTA. *Minerva medica* [*Minerva med.* (*Torino*)] **1**, 1205–1217, April 21, 1956. 14 figs.

The authors report the results of treatment with daily intravenous infusions of ACTH in combination with antibiotics in 60 cases of pulmonary tuberculosis. They started with a dose of 5 mg. of ACTH and gradually decreased the amount to 1 mg. or 0·5 mg., 37 to 67 perfusions being given, with a total dosage of up to 272 mg. of ACTH. The perfusions were usually well tolerated. Streptomycin was given concurrently in doses of 1 g. daily; was used isoniazid, with or without PAS, only in cases of intolerance to streptomycin, both drugs being given in the highest dosage tolerated by the patient. According to the authors the results were "excellent" in 18 cases, "good" in 14, and "moderate" in 6, while 10 cases were not influenced at all. (The various factors to be considered in the assessment of the results of treatment are discussed in detail, and a number of illustrative cases are described.) In 12 cases the treatment had to be discontinued on account of side-effects.

The authors recommend treatment with ACTH for proliferative and exudative forms of pulmonary tuberculosis and after surgical intervention, especially in cases in which chemotherapy alone has proved ineffective.
Franz Heimann

1121. **The Endotracheal Treatment of Bronchopulmonary Tuberculosis.** (La via broncoinstillatoria nel trattamento della tubercolosi broncopolmonare)
A. FERRARIS and G. CHIODI. *Minerva medica* [*Minerva med.* (*Torino*)] **1**, 1217–1220, April 21, 1956. 18 refs.

An account is given of the treatment of 20 patients suffering from bronchopulmonary tuberculosis with endotracheal instillations of a preparation containing streptomycin and isoniazid, given through a Métras catheter after local anaesthesia had been established. Each patient received an average of 15 instillations at intervals of 15 to 30 days. No toxic side-effects were observed. According to the authors a good clinical recovery was obtained in 9 cases, moderate improvement was recorded in 6, and in 5 the treatment had no influence at all. *Franz Heimann*

1122. **The Treatment of Tuberculous Lung Cavities by Continuous Intrapulmonary Drip. A Preliminary Report**
D. J. M. JENKIN. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 181–186, April, 1956. 8 figs., 2 refs.

Monaldi's technique of draining a tuberculous cavity by the introduction of a catheter has been used by the author at the King George V Hospital, Durban, to irrigate tuberculous cavities persisting in patients with a positive sputum after prolonged medical treatment. Solutions containing 1,500 or 3,000 mg. of isoniazid in 60 or 120 ml. of fluid respectively, to which were added 5 g. of streptomycin, 1,000,000 units of penicillin, and 1 g. of oxytetracycline, were instilled through the catheter in a slow continuous drip for up to 8 hours once or twice a week until healing of the cavity occurred. This treatment was augmented by the parenteral administration of streptomycin and isoniazid. The intrapulmonary drip at first resulted in distressing and exhausting cough, local spread of infiltration, and loss of weight, but with each treatment the reaction was less severe. Improvement followed, with reduction of sputum, recovery of lost weight, and in 3 out of 8 cases complete closure of the cavity, with partial closure in some of the others in which treatment is still proceeding and in which satisfactory results are confidently anticipated by the author. Contraindications to the procedure are inaccessibility of the cavity to intubation and the presence of a free pleural space.
J. Robertson Sinton

1123. **A Pathologic and Bacteriologic Study of Cavitary Pulmonary Tuberculosis Treated with Streptomycin and Isoniazid**

J. DENST and W. F. RUSSELL. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **26**, 335–344, April, 1956. 8 figs., 12 refs.

In this paper from the University of Colorado School of Medicine, Denver, the authors compare the bacteriological and histological findings in lung specimens containing tuberculous cavities resected from two groups of patients: (1) 33 patients who had received a long-term course of treatment with streptomycin and isoniazid given together and 24 who had received a short initial course of streptomycin in high dosage followed by a prolonged course of isoniazid; and (2) a control group of 25 patients who had been treated with streptomycin and PAS only and 10 who had died without specific treatment.

There was a close cultural correlation between the organisms obtained from the sputum and those isolated from the surgical specimens; in 9 patients who had negative sputum cultures at the time of operation, cultures from the cavity wall were also negative. Bacterial resistance to isoniazid usually appeared after 2 months, while resistance to streptomycin developed more slowly and started later.

The histology of cavities containing tubercle bacilli varied widely, but extensive liquefaction of necrotic tissue with abundant haemorrhagic or purulent material was usually present or there was a thin pyogenic membrane adherent to the lining. In contrast to the findings in the controls there was a discrete zone of haemorrhage in the wall in 76% of cases treated with isoniazid. Microscopically, the lining consisted of thick, well vascularized granulation tissue infiltrated with plasma cells and lymphocytes, often with a wide zone of epithelioid cells and giant cells. Vascularization of the cavity wall was most marked in cases in which the organism was resistant to both drugs. "Extracavitary, atypically located, highly pleomorphic giant cells and clusters of large mononuclear cells" were common in the cases treated with isoniazid, but these cells were noted in only 2 of the control cases. In 5 cases endogenous spread by isoniazid-resistant organisms had occurred. The 10 cavities from which no drug-resistant bacilli were isolated showed changes suggestive of complete healing and transformation into cyst-like cavities with smooth walls.

The 9 patients in whom sterilization of the cavity had occurred had been under treatment for 7 to 15 months. Sterilization of the cavity is probably followed by elimination of the caseous material, the wall passing through a highly cellular stage in which the appearances resemble those of a foreign-body reaction. Finally a thick, fibrous membrane remains. The more rapid emergence of isoniazid-resistant organisms suggests that isoniazid acts freely on organisms within the cavity, whereas streptomycin fails to do so. Once resistance appears, if the cavity is still open, surgery is indicated.

(It was found incidentally during this study that with a standard dosage of isoniazid the blood level of the drug varies widely in different patients.)

F. Hillman

1124. **A Five-year Assessment of Patients in a Controlled Trial of Streptomycin, *para*-Aminosalicylic Acid, and Streptomycin plus *para*-Aminosalicylic Acid, in Pulmonary Tuberculosis**

W. FOX and I. SUTHERLAND. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 221–243, April, 1956. 1 fig., 4 refs.

In this paper are reported the results of a 5-year follow-up study of 166 patients included in the Medical Research Council's second controlled clinical trial of chemotherapy in pulmonary tuberculosis. The patients, who were young adults aged 15 to 30 years with acute progressive bilateral disease of recent origin, unsuitable for collapse therapy, were admitted to hospital for 6 months' treatment and then allocated at random to a 3-month course of chemotherapy. Streptomycin, 1 g. daily, was given to 54 patients (Group S), PAS (sodium salt), 20 g. daily, to 59 patients (Group P), and a combination of these two drugs to 53 patients (Group SP). The distribution of cases according to clinical condition on admission was similar in the three groups, except that in Group SP there were rather fewer cases of very severe disease. At the end of the 3-month period the clinician was free to give any treatment he wished to the patients in any group, and this additional chemotherapy and collapse therapy had an important bearing on the interpretation of the long-term results.

Comparatively few patients in Group S received additional treatment compared with over half the patients in Group P. At the end of 5 years 17 patients in Group S, 21 in Group P, and 10 in Group SP had died. The disease process was arrested or quiescent in 28 patients in Group S, 32 in Group P, and 37 in Group SP. The differences between the sexes in mortality and disease status were unimportant. Of special interest was the finding that although at the end of 6 months' treatment the radiological appearances in Group P were less favourable than those in Group S, no statistical difference in this respect was observed between the two groups at the end of 5 years, this being attributed to the additional treatment given to Group P. Group SP also received more treatment than Group S and the favourable findings in the former at the end of 5 years were probably related to this factor. When the three groups were combined it was found that of 134 patients surviving at the end of 2 years 68% had no working capacity and of 118 surviving at 5 years the percentage of such patients was 14. At 5 years cavitation was visible in a standard radiograph also in 14% of the 118 survivors.

Analysis of the clinical features on admission showed that involvement of all 6 lung zones was a poor prognostic sign in all 3 groups. There was only slight correlation between the erythrocyte sedimentation rate and the mortality in each of the 3 groups. Extensive cavitation, high pyrexia, lack of radiological improvement, a positive sputum after 3 months, and the emergence of organisms resistant to streptomycin or PAS within the first 6 months were unfavourable prognostic signs in Groups S and P.

A comparison, as regards 5-year progress, of the 54 patients initially given streptomycin only in this trial and the 55 given similar treatment in the first Medical

Research Council trial revealed " a considerable benefit to the later series, attributable to more additional chemotherapy and major surgical measures, as well as to a fuller understanding . . . of the application of chemotherapy and surgery ". *I. Ansell*

1125. **The Treatment of Bronchopulmonary Tuberculosis with Antibiotics Administered by the Bronchial Route.** (Traitement de la tuberculose broncho-pulmonaire au moyen d'antibiotiques administrés par voie bronchique) M. POPPER, S. DAVIDSONN, Y. ESKENASY, and M. FINKELSTEIN. *Journal français de médecine et chirurgie thoraciques* [*J. franç. Méd. Chir. thorac.*] **10**, 22–37, 1956. 22 figs.

In this communication from the Faculty of Medicine, Bucharest, the authors describe the results in 250 cases of pulmonary tuberculosis treated with instillations of antibiotics into the bronchial tree by the following method. After anaesthetization of the air passages with 2% cocaine or 1% amethocaine a catheter is inserted under *x*-ray control into the diseased area of the lung. The patient is postured so that the diseased area is dependent and the antibiotic solution, preferably heated to 35° C., is introduced slowly over some 5 to 10 minutes. The patient remains in the same posture for one hour after the instillation. This treatment was given three times weekly and continued for periods ranging from 30 to 90 days. The authors found that 0·5 g. of streptomycin with 0·3 to 0·5 g. of isoniazid was the most effective combination of drugs. Two cases of bronchogenic spread occurred and there were some minor upsets such as loss of appetite and digestive disturbance; in a few cases mental changes thought to be due to the anaesthetic employed were prevented by small doses of phenobarbitone.

The authors consider that drugs given by this method act in four ways: (1) by mechanical relief of bronchial obstruction; (2) through a reflex originating in the broncho-pulmonary receptors which modifies bronchial tone; (3) by a local antibiotic action; and (4) by a general antibiotic action. Laboratory studies showed that in patients with diseased lungs the concentration of antibiotics in the blood at the end of 24 hours was similar to that obtained by parenteral administration.

For assessment of the results the patients were divided into six groups. (1) Of 123 patients with proved endobronchial tuberculosis, the condition was " cured " in 120. The accompanying fibro-caseous lesions were also affected, being cured in 43 cases, improved in 67, and unchanged in 13. (2) Of 56 cases of residual cavity after thoracoplasty or extra-pleural pneumothorax, 17 were cured, 25 improved, and 14 unchanged. (3) Of 22 patients with tension cavities, 12 were cured, 8 improved, and 2 unchanged. (4) In 14 cases there were cavities in the apex or base of the lower lobes which the authors considered unsuitable for treatment by collapse therapy; of these, 7 were cured, 4 improved, and 3 unchanged. (5) Of 27 cases of bilateral disease unsuitable for collapse therapy, 18 were so much improved that this procedure could eventually be carried out, and 9 were unchanged. (6) Lastly, of 7 patients with recent cavitation who had had no previous treatment, 4 were cured, 2 improved, and in one the cavity closed but reopened at a later date. Of the whole group, sputum conversion occurred in 70% within 25 to 40 days and the sputum remained negative for 3 years after the end of treatment. *G. M. Little*

1126. **Five-year Follow-up of Minimal Pulmonary Tuberculosis with and without Chemotherapy**
M. E. FLOREY. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 818–830, June, 1956. 2 figs., 8 refs.

In this paper from the Sir William Dunn School of Pathology, Oxford, the author reports the further progress of 30 of the 37 patients with minimal pulmonary tuberculosis who were the subject of a clinical trial started at the Central Middlesex Hospital in 1948 as previously described (*Amer. Rev. Tuberc.*, 1952, **65**, 547; *Abstracts of World Medicine*, 1952, **12**, 405). Of the original 37 patients, 18 received no chemotherapy of any kind and 19 were treated with streptomycin in doses of 1 g. daily for up to 4 years; 15 of these patients in each group have now been followed up for 5 years.

Of those treated without chemotherapy, 11 are well and active, 5 developed pleural effusion or relapsed, and in 3 a new cavity developed or an old cavity persisted. Of the 15 in the streptomycin-treated group, 12 are well and active, 3 relapsed, and 3 developed cavities, but there were no cases of effusion. In only one case did the organisms become resistant to a concentration of streptomycin greater than 10 μg. per ml. A considerable number of the patients who did not receive streptomycin were given collapse therapy and the author discusses the value of this treatment. She concludes that streptomycin is more effective.

[The numbers in this trial are too small to allow of any firm conclusions being drawn. Nevertheless the trial is of historical interest in that it deals with cases of tuberculosis treated with streptomycin when it alone of the now currently used antituberculous chemotherapeutic agents was available.] *I. M. Librach*

1127. **The Changing Place of Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis**
P. ELLMAN, J. H. P. JOHNSON, and A. KAGAN. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 130–151, April, 1956. 5 figs., 40 refs.

The authors review the results in 152 patients with pulmonary tuberculosis who were treated with artificial pneumothorax (A.P.) at Plaistow Hospital and East Ham Chest Clinic, London, before the introduction of chemotherapy. The results were similar to those of other investigators in that 68% of the patients have done well, 8 (5·7%) of the 140 followed up have died, and 10 more were presumed to be dead, giving a maximum death rate of 12%. The incidence of fibrothorax and incomplete re-expansion, even when arrest of the disease was achieved, was of the order of 15%. Segmental atelectasis did not alter the prognosis, but major atelectasis, together with a persistent tension cavity, pleural effusion, empyema, and extensive contralateral disease,

were major factors in the production of poor results. A prolonged A.P., in the absence of pleural complications, did not appear to prevent satisfactory re-expansion of the lung, as judged radiologically.

Pointing out that the addition of chemotherapy is likely to prevent most of the complications of pneumothorax, the authors conclude that there is still a place for this form of collapse therapy in the treatment of patients with upper-zone exudative lesions (with or without cavitation) which fail adequately to respond to rest, posture, and chemotherapy, and also of some young patients in whom, after an adequate response to treatment, the induction of pneumothorax will provide supportive therapy in the presence of low natural resistance.

J. Robertson Sinton

1128. **Tuberculous Hypotension**

R. G. BENIANS. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 152–158, April, 1956. 7 figs., 12 refs.

The author has investigated the blood pressure in 191 patients with pulmonary tuberculosis at the Bradford Chest Clinic and St. Luke's Hospital, Bradford. Accepting a figure of 100 mm. Hg as a normal mean arterial pressure, he found that while most patients suffering from pulmonary tuberculosis involving less than three " radiological zones " had a normal mean arterial pressure, in 47 patients (22·5%) with more extensive disease the mean arterial pressure lay between 70 and 90 mm. Hg. Low pressures tended to rise during treatment, but in only a few cases did they reach a normal level.

The series included 5 patients with extensive pulmonary disease and a low mean arterial pressure, but no definite stigmata of Addison's disease of the adrenal glands. In these patients adrenal function was investigated by the Kepler water-load test, Thorn's test (eosinophil-count depression after administration of ACTH (corticotrophin)), and the effect on the urinary excretion of 17-ketosteroids and 17-ketogenic steroids of stimulation with ACTH. The result of the Kepler test was positive in 2 cases and negative in 3, while Thorn's test showed eosinopenia in 4 cases, but the excretion of steroids after ACTH indicated that adrenal function was normal. It is concluded that hypotension is common in patients with tuberculosis, but that there is no evidence that adrenal dysfunction is the cause of this hypotension.

J. Robertson Sinton

1129. **The Course of Tuberculosis Immediately after the End of Pregnancy.** (Tuberkuloseabläufe kurz nach Schwangerschaftsbeendigung)

H. W. GIERCKE. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] 108, 1–8, 1956. 13 figs.

Of 930 pregnant women with a history of tuberculosis seen at the Waldeck Sanatorium near Rostock, East Germany, in the last 5 years, 774 went to full term and 33 were delivered prematurely; there were 35 cases of abortion and in 88 pregnancy was interrupted. Out of the 930 patients, 90 showed deterioration of their tuberculosis within 6 weeks of the end of pregnancy—that is, in the period covered by this report—all but 6 of whom suffered from pulmonary tuberculosis. Of these 90 patients, 70 had been considered to show no sign of active disease during pregnancy.

[Since no details are given either of the criteria of activity of the disease or of any treatment given to the patients, assessment of the results is difficult.]

P. Mestitz

1130. **Serum Proteins in Pulmonary Tuberculosis**

I. C. GILLILAND, R. N. JOHNSTON, P. STRADLING, and E. M. ABDEL-WAHAB. *British Medical Journal* [*Brit. med. J.*] **1**, 1460–1464, June 23, 1956. 6 figs., 11 refs.

The authors have studied the serum protein fractions in 327 adult patients with pulmonary tuberculosis at the Hammersmith Chest Clinic (Postgraduate Medical School of London) with particular reference to the relationship between changes in the serum protein pattern and the extent, duration, and severity of the pulmonary lesion, and also the effect of chemotherapy. The total protein concentration in each serum specimen, obtained from venous blood samples, was estimated by the specific gravity method and the protein fractions assessed quantitatively by scanning with a densitometer after separation by electrophoresis on filter paper. The experimental technique is described in detail. The paper strips were dried in an oven at 120° C. for 30 minutes, stained by immersion for 10 minutes in 0·2% lissamine green SF150 in 15% acetic acid, and washed with 2% acetic acid until the background of the strip was white. After scanning, the areas of the resulting recordings were measured by planimetry and the relative concentrations of the protein fractions calculated.

The patients were selected initially without reference to their clinical condition, but a clinical assessment was made at the time the blood samples were obtained and was based on five main factors: (1) extent of the disease as assessed radiologically and using the " zone system " of the Ministry of Health; (2) approximate duration of the disease, subdivided into (*a*) recent infection (under 6 months), (*b*) intermediate (6 months to 3 years), and (*c*) disease present for over 3 years; (3) activity of the disease, classed as active, quiescent, arrested, or intermediate; (4) the duration and type of treatment already received; and (5) special factors, such as co-existing amyloidosis or diabetes mellitus. In addition, 28 of the patients' adult contacts who were radiologically free from tuberculous disease and living in a similar domestic environment were examined, and served as a control group.

The results showed that the serum albumin concentration fell and the α_2-globulin concentration rose progressively with increasing extent and activity of the disease, and that the values for these fractions moved towards normal as treatment with antituberculous drugs took effect and as the disease became quiescent or arrested. The authors suggest that the ratio of albumin to α_2 globulin in the serum is the most sensitive single index of changes in the serum proteins and provides a much more useful objective index for assessing the activity of disease in patients with tuberculosis than the erythrocyte sedimentation rate. *M. J. H. Smith*

Venereal Diseases

1131. **Venereal Disease and the Homosexual**
F. J. G. JEFFERISS. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 17–20, March, 1956. 2 figs., 3 refs.

The author discusses certain aspects of the problem of the male homosexual and shows that a significant proportion of male patients with venereal disease are homosexual. Of 1,000 consecutive male patients with gonorrhoea or early syphilis who attended St. Mary's Hospital, London, in 1954, 84 (8·4%) admitted recent sexual contact with another male. Omitting 255 coloured patients, of whom 4 were homosexual, there were left 745 white patients, of whom 80 (10·7%) were homosexual. Analysis of the figures by marital status revealed that 15·7% of the single white men were homosexual and analysis by occupation showed that the corresponding figure for white unmarried non-manual workers was 23·2%. Taking into account the number of patients who may have been unwilling to admit the source of their infection, the author suggests that even these high figures may be too low.

A more detailed study of a group of 224 homosexual patients seen in the past 2½ years showed that 164 had gonorrhoea, 10 had early syphilis, 16 non-gonococcal urethritis, and 34 other conditions. The age incidence varied from 13 to 67 years; 97 men said that they usually played a passive and 127 an active role, while 24 were what they called " versatile ". Of these 224 patients, 113 had ano-rectal disease and 116 urethral disease, 5 having both, the total number of infections, including re-infections, being 477. There were only 8 married men in this series. Inquiry as to occupations showed a predominance of clerks, shop-assistants, waiters, and those employed in the artistic trades.

Of a selected group of 54 patients who were examined more fully and interviewed, 40 (74%) came from broken homes, 23 of these (42% of the total) having been brought up by the mother only; only 14 (26%) came from normal, happy homes. The patients came from varying sizes of family and from all social classes, and usually did not know of other homosexuals in the family. They showed no obvious physical or endocrine change except in one case. The great majority (46 (85%)) had been to day schools and only 8 (15%) to boarding schools. Moreover, all the latter stated that they had their first homosexual experience after leaving school.

The author divides homosexuals into two groups, the " congenital " and the " acquired ". The former group, which he believes is not amenable to any influence or treatment, includes the true inverts and those in whom homosexuality might be considered to be inborn. In the " acquired " group, which numbered only 3 cases in the selected series, he places those who have little or no inborn leaning towards homosexuality, but have been influenced by others or by circumstances to practise it.

Benjamin Schwartz

1132. **Venereal Disease Control in New York City**
T. ROSENTHAL and J. E. VANDOW. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **71**, 381–390, April, 1956. 5 figs., 11 refs.

Statistical recording of venereal disease morbidity in New York City has been standardized since 1938, and in the present paper the information collected since then is reviewed. During the period 1938 to 1941—that is, before the advent of penicillin—the number of reported cases of syphilis declined from 37,077 a year (503·6 per 100,000 population) to 27,194 (362·1 per 100,000). However, the number of reported cases of gonorrhoea, some 13,000 a year (175·7 per 100,000 population) changed little during the period, while the number of cases of chancroid in 1941 (5·7 per 100,000) was 2½ times higher than it was in 1938.

During the years 1941 to 1945 the incidence of primary and secondary syphilis increased over 40% and of latent syphilis over 20%, particularly in the younger age groups. The number of cases of gonorrhoea also rose steeply from 163·7 to 234·4 per 100,000 population. Peak levels for notified cases of both syphilis and gonorrhoea were reached in 1946, after which there was a steady fall. In 1954 the number of cases of syphilis had fallen to 19,412 (241·4 per 100,000). Of these, primary or secondary infection was present in only 617 and early latent infection in 2,183. In the same year 12,379 cases of gonorrhoea were reported (153 per 100,000). There was a similar decline in the incidence of other venereal diseases, which, however, had never been a great problem in New York City, but the number of cases of non-gonococcal urethritis (admitted to Health Department clinics for the first time in 1951) rose to 1,238 cases (15·3% of all cases of urethritis).

The success of the venereal diseases control programme in New York City is considered to be due to the skilful combination by the official health agencies of the resources of private practitioners and hospital staffs, educational institutions, social and welfare services, voluntary health organizations, the clergy, and the Services. Further reductions in the incidence of venereal diseases will, however, be difficult to achieve in an area with such a shifting population as New York City.

Benjamin Schwartz

1133. **Treatment of Gonorrhœa with Phenoxymethylpenicillin by Mouth.** (Tratamiento de la gonococia con penicilina (ácido penicilínico V) por vía oral))
X. VILANOVA and A. ZUBIRI. *Actas dermo-sifiliográficas* [*Act. dermo-sifiliogr. (Madr.)*] **47**, 571–575, April, 1956 [received July, 1956]. Bibliography.

The authors describe experiments in which 4 volunteer subjects were given 120 mg. (300,000 units) of phenoxymethylpenicillin (" penicillin V ") by mouth, the first receiving the antibiotic one hour after food, followed

after a further hour by the introduction into the anterior urethra of gonococcal pus from an acute case of gonorrhoea. The second subject received the penicillin fasting and the urethral inoculation with pus was given 30 minutes later. In neither of these cases did urethral smears [repeated over an unstated period] show any evidence of gonorrhoea. In the third subject the pus was inserted at the same time as he was given oral penicillin, and in the fourth 55 minutes before the antibiotic; urethral smears examined at 24 hours and 7 and 11 days after inoculation again showed no evidence of gonorrhoea in either of these 2 subjects.

In a clinical trial 3 cases of acute gonococcal urethritis were treated with 480 mg. (8 tablets or the equivalent of 1·2 mega units) of phenoxymethylpenicillin given during a 15-hour period to ensure a serum penicillin level of at least 0·2 Oxford units per ml. for 24 hours. Nine hours from the start of treatment urethral smears no longer contained gonococci; further smears gave negative results at 9 days after treatment in the first case, at 12 days in the second, and at 3 days in the third.

[In discussing the advantages of oral penicillin the authors comment that many patients try to avoid injections which are inconvenient and which "require the intervention of another person". However, if the use of oral penicillin is not very carefully controlled by the physician most undesirable results may ensue.]

Eric Dunlop

SYPHILIS

1134. **Untreated Syphilis in the Male Negro. Twenty-two Years of Serologic Observation in a Selected Syphilis Study Group**

S. OLANSKY, A. HARRIS, J. C. CUTLER, and E. V. PRICE. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] 73, 516–522, May, 1956. 2 figs., 10 refs.

A further report on the Tuskegee study of untreated syphilis in the male negro, which was begun in 1932, is presented. No serological data are available for the period 1932 to 1939, but since 1939 serological examinations have been attempted annually, the last being completed in 1954. The present analysis is confined to the results obtained with the Kahn standard test for syphilis, which has remained relatively unchanged during the 22-year period. The subjects included 408 men originally selected as syphilitic in 1932, 10 of 201 controls who later acquired the disease, and 13 syphilitics added in 1939. Of the 431, 176 (40·8%) were dead and only 93 (36·5%) of those presumed to be alive were examined in 1954. Altogether, 299 were followed up serologically for varying periods, 76 died before they could be re-examined, and 56 were untraced.

Among the 175 untreated patients—that is, patients who had had no antisyphilitic treatment or fewer than 3 injections of arsenic—the rate for serological reversal to negative was lowest in those aged 25 to 39 years with syphilis of less than 15 years' duration, the highest rate being found in patients aged 55 to 69 years with syphilis of 30 to 44 years' duration. The more recently acquired the infection, the longer the time required for serological reversal to negative. However, only a very little treatment was necessary to reverse this pattern. Patients aged 25 to 39 years with syphilis of less than 15 years' duration treated with 3 to 20 arsenic injections had the highest seronegativity rate. Similar treatment given to patients 40 to 54 years of age with syphilis of 15 to 29 years' duration had no apparent effect.

Leslie Watt

1135. **Inoculation Syphilis in Human Volunteers**

H. J. MAGNUSON, E. W. THOMAS, S. OLANSKY, B. I. KAPLAN, L. DE MELLO, and J. C. CUTLER. *Medicine* [*Medicine* (*Baltimore*)] 35, 33–82, Feb., 1956. 2 figs., bibliography.

The authors describe in great detail an experiment carried out on 8 non-syphilitic men, 49 with treated syphilis, and 5 with untreated latent syphilis, all of whom were volunteers from Sing Sing Prison, New York State.

First, 24 of the patients were inoculated with 50×10^6 heat-killed *Treponema pallidum* and followed up by means of bi-weekly clinical and serological examinations for 6 weeks. All 62 patients were then inoculated with virulent *T. pallidum* (Nichols strain). The 54 syphilitic subjects received 10^5 organisms, while the 8 non-syphilitic patients were each given four doses, of 10, 10^2, 10^3, and 10^4 organisms respectively, at four different sites. All injections were given intracutaneously into the skin of the forearm. Treatment was withheld for 4 months unless dark ground positive lesions developed or there was a sustained rise in the standard serological test (S.T.S.) titre, when 1·2 mega units of penicillin in aluminium monostearate was administered daily for 5 days.

As calculated by the Bliss dose–response technique, the 50% infectious dose (ID_{50}) in the non-syphilitic individuals was found to be approximately 57 organisms. A parallel experiment in rabbits in which the same suspension was used gave an ID_{50} of 23 organisms, showing that the Nichols strain of treponeme (which has been maintained by passage in rabbits since it was first isolated in 1912) still retains a high virulence for man.

Of the 54 syphilitic patients, 2 were discarded from the experiment as penicillin had to be given for other reasons before the result of the inoculation was known. The 5 patients with untreated latent syphilis showed no clinical or serological response. All the remaining patients had received adequate treatment before being accepted for the experiment. Of 11 who had been treated for early syphilis, 9 developed darkground (D.G.)-positive lesions and 2 D.G.-negative lesions. The S.T.S. titre rose in all 11 cases, and it was noted that both the S.T.S. and the treponemal immobilization (T.P.I.) titres rose more rapidly than in the non-syphilitic controls. Of 3 patients who had been treated previously for re-infections, one developed a D.G.-positive and one a D.G.-negative lesion, the S.T.S. titres rising in both, while the third patient showed no clinical or serological response. Out of 26 patients with treated late latent syphilis, 13 showed no response to the inoculation and 3 further patients developed D.G.-negative lesions with-

out any rise in the S.T.S. titre. Ten patients were thought to have been re-infected; all showed a rise in S.T.S. titre, one a D.G.-positive lesion, and 9 D.G.-negative lesions, one of these being gummatous. Of 5 patients who had been treated for congenital syphilis, one showed no response to the inoculation, a D.G.-positive lesion developed in another, and D.G.-negative lesions associated with increased S.T.S. titres in the remaining 3, the lesion being gummatous in one case. One of 2 patients with treated asymptomatic neurosyphilis showed no response, while the other complained of headaches and nervousness 3 months after inoculation and his spinal fluid showed a slightly raised cell count. There was no change in the S.T.S. or T.P.I. titres in this case and it was not possible to confirm the previous treatment he claimed to have received.

In the group of patients who received the preliminary inoculation of heat-killed organisms there was an anamnestic rise in the T.P.I. titre in some patients who had been treated for early syphilis, but there was no rise in the S.T.S. titre; no immobilizing antibody developed in the 3 non-syphilitic control patients who received the same inoculum. The authors suggest that the administration of the killed antigen may have had a " booster " effect on the immunity to re-infection of some patients previously treated for syphilis.

[Some eight pages of this paper are devoted to a review of previous work on experimental syphilitic infection in man.] *A. E. Wilkinson*

1136. **Significance of the *Treponema pallidum* Immobilization Test on Spinal Fluid**

J. L. MILLER, M. H. SLATKIN, and J. H. HILL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1394–1397, April 21, 1956. 5 refs.

The validity, within certain limitations, of the *Treponema pallidum* immobilization (T.P.I.) test on blood is now generally accepted. The authors have therefore attempted to evaluate the validity of this test on the cerebrospinal fluid (C.S.F.), and in this paper report the results of the T.P.I. test and a standard serological test for syphilis on 376 specimens of C.S.F. from 324 patients, most of whom were attending the Columbia University–Presbyterian Medical Center, New York. The same tests were also performed on the blood of all but 31 of these patients.

Of the total number, 173 patients were diagnosed as having latent syphilis [but no results of the T.P.I. test on the C.S.F. in this group are given], and 54 patients had clinical evidence of neurosyphilis (26 cases of tabes, 7 of paresis, 12 of meningovascular syphilis, and 9 of primary optic atrophy). Positive or doubtful T.P.I. test results were obtained in all but 8 cases, while 5 patients with tabes gave a negative T.P.I. reaction with the C.S.F. but a positive reaction with the blood. The same pattern was found in one case of treated paresis and in 2 patients with optic atrophy. In 46 cases a diagnosis of asymptomatic neurosyphilis was made, the T.P.I. test on the C.S.F. giving a positive result in 36 and a doubtful result in 4. The 6 remaining patients, 5 of whom had had antisyphilitic treatment, showed a negative T.P.I. reaction in the C.S.F., while the standard test on the C.S.F. and both tests on the blood gave positive results.

Thus in the combined group of 100 patients with neurosyphilis, the T.P.I. reaction in the C.S.F. was negative in 14 cases. In the same group the standard test result on the C.S.F. was negative in 16 instances, but in 12 of these the T.P.I. reaction with the C.S.F. was positive. The authors state that all the positive T.P.I. test results on the C.S.F. were in agreement with the clinical diagnosis and suggest that this finding is good evidence of neurosyphilis, but point out that failure to demonstrate immobilizing antibody in the C.S.F. does not rule out the diagnosis of neurosyphilis.

Tests on 18 patients showed that the antibody titre was always lower in the C.S.F. than in the blood. It was also noted that when 49 T.P.I.-positive specimens of C.S.F. were re-tested after deep-freeze storage, 3 gave negative results at the second examination; 2 of these specimens had been stored for one month and one for 15 months. This reversal of the reaction is probably related to a low titre of antibody. *A. E. Wilkinson*

1137. **Resistance of Specifically-sensitized *Treponema pallidum* to Methylene Blue Stain**

B. J. ROSENAU and J. F. KENT. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 579–582, April, 1956. 8 refs.

Work at the Walter Reed Army Institute of Research, Washington, D.C., has shown that virulent *Treponema pallidum*, which is normally stained by methylene blue, becomes resistant to such staining when incubated with syphilitic serum and complement. The authors have therefore explored the possibility of utilizing this phenomenon in the diagnosis of syphilis. Their method is as follows.

A mixture of serum, a suspension of living treponemes (Nichols strain), and active and inactive complement is incubated as in the treponemal immobilization (T.P.I.) test. About 0·01 ml. of the reaction mixture is then placed on a slide, an equal volume of a stain composed of 0·1% methylene blue and 0·025% sodium carbonate in distilled water is added, and a coverslip applied. The preparation is left at room temperature for 15 minutes and examined by dark-ground illumination. The percentages of stained treponemes in the presence of active complement and in the mixture with inactivated complement as a control are counted, from which the " specific dye resistance " (S.D.R.) is calculated in a similar way to the calculation of specific immobilization in the T.P.I. test. Sera showing more than 50% S.D.R. are assessed as reactive, from 21 to 50% as weakly reactive, and less than 21% as non-reactive. After the reading, tests to demonstrate the presence of residual complement are performed as in the T.P.I. test.

Application of the method to examination of syphilitic rabbit serum showed that active complement was required for the manifestation of dye resistance and that the titre by this technique paralleled that of immobilizing antibody. Removal of reagin from the serum by absorption

with cardiolipin antigen had no effect on the dye-resistance titre. Duplicate tests on 169 selected sera from healthy subjects, patients with syphilis, and patients with diseases other than syphilis showed very close agreement between the results of the T.P.I. test and the dye-resistance test. Attempts to use suspensions of *T. pallidum* killed by a variety of treponemicidal agents were generally unsuccessful. It was noted that exposure to a temperature of 56° C. for 10 minutes frequently immobilized the treponemes without altering their capacity to resist the dye, but this effect was not predictable.

A. E. Wilkinson

1138. **A Comparative Study with Cardiolipin Antigen of the Flocculation and Kolmer Complement-fixation Reactions.** (Vergleichende Luesuntersuchungen mit dem Cardiolipin-Antigen in der Flockungs- und Komplementbildungs-Reaktion nach Kolmer)

A. GAASE. *Zeitschrift für Immunitätsforschung und experimentelle Therapie* [*Z. ImmunForsch.*] **113**, 154–163, April, 1956, 11 refs.

In a comparative study carried out at the Municipal Serological Institute, Bochum, Germany, 1,111 sera were tested with cardiolipin antigen by means of the flocculation and Kolmer complement-fixation reactions and the results compared with those of the classic Wassermann, Meinicke, and citochol reactions. The Wassermann test proved the least sensitive, while the two reactions using cardiolipin antigen were both more sensitive and specific than the other tests used. It is recommended that both these tests should become routine procedures. The samples of serum originated from treated syphilitics in 432 instances, but since the remaining 679 specimens were received without clinical details the problem of false positive reactions could not be assessed.

G. W. Csonka

1139. **Oxytetracycline Intramuscular in the Treatment of Early Syphilis**

G. R. BALER. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 489–492, May, 1956. 17 refs.

In the hope of finding a substitute for penicillin in the treatment of cases of early syphilis with allergic reactions, oxytetracycline was tried at the Davidson County Health Department, Nashville, Tennessee. Crystalline oxytetracycline in a solution containing magnesium chloride and 2% procaine hydrochloride was given by intramuscular injection to 16 patients with early syphilis (primary infection in 2 and secondary in 14). The dosage in 15 cases was 200 mg. twice daily for 10 days and in one case it was 100 mg. twice a day for 3 days followed by 200 mg. twice a day for 7 days (total 3·4 g.).

All lesions healed rapidly after the start of treatment, *Treponema pallidum* disappearing in an average of 40 hours. The patients were followed up for 8 to 16 months. In 4 cases treatment was a failure: there was a mucocutaneous relapse after 4 months in one case and serological relapse in 2 cases after 6 and 10 months respectively; in one case, in which initially the cerebrospinal fluid findings were positive, there was an inadequate response, as indicated by a persistently high serological titre, although the cerebrospinal fluid findings were negative after 7 months. One patient with secondary infection was delivered of a full-term normal infant 119 days after the start of treatment; response to the V.D.R.L. test in this infant continued to be negative after 2 months. There were no major reactions to this treatment.

The results in this small series of cases indicate that oxytetracycline given intramuscularly is at least as effective in the treatment of early syphilis as are the other broad spectrum antibiotics; its efficacy, however, does not approach that of penicillin. Further investigation with a higher total dosage is recommended.

Leslie Watt

1140. **Penicillin in Late Latent Syphilis. Results of Therapy with Procaine Penicillin in Aluminum Monostearate**

M. L. NIEDELMAN. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 503–509, May, 1956. 7 refs.

The investigation described in this paper from the General and Temple University Hospitals, Philadelphia, was undertaken to evaluate the therapeutic efficacy of penicillin in late latent syphilis, a review of the literature indicating that such investigation was necessary. The author defines late latent syphilis as asymptomatic syphilis of more than 4 years' duration in which there is no clinical or laboratory evidence of the disease except for a positive response to serological tests. In this investigation the Kahn complement-fixation test and the Kahn and V.D.R.L. quantitative serum tests were performed. All patients known to have congenital syphilis were excluded, and every precaution was taken to exclude biological false positive reactions.

A total of 316 patients, the majority of whom were females and about one-half between 20 and 50 years of age, were followed up for periods of 1 to 3 years after initial treatment. Penicillin with aluminium monostearate was given in a dosage per course of between 3,600,000 and 6,000,000 units. The best results, as indicated by the number of patients who gave a negative response to serological tests or showed a satisfactory titre (4 to 8 Kahn units), were obtained in those who had previously received adequate bismuth and arsenical therapy (28 out of 38 patients). Next came those who had had inadequate metallotherapy (36 out of 60) and those who had not previously been treated (103 out of 188). Treatment was unsatisfactory in 23 of the 30 patients who had had penicillin therapy previously—that is, the re-treatment group. The author states that after the titre had fallen to a satisfactory level further treatment had no appreciable effect. Altogether there was a negative response or a satisfactory titre after treatment in 170 of the 316 patients (53·8%), although before treatment the titre had been satisfactory in only 93 (29·5%).

The author concludes that penicillin is as effective in the treatment of late latent syphilis as arsenic and bismuth. There was no progression of the disease in any of the patients during the time of the study.

Leslie Watt

Tropical Medicine

1141. **Fatal Amebiasis: Report of 148 Fatal Cases from the Armed Forces Institute of Pathology**
B. H. KEAN, H. R. GILMORE, and W. W. VAN STONE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 831–843, May, 1956. 29 refs.

From Cornell University Medical College, New York the authors report a study of the clinical and pathological features of fatal amoebiasis based on case records filed at the Armed Forces Institute of Pathology, Washington, D.C., between 1862 and 1953. During this period there were 290 fatal cases of amoebiasis, and 148 of these, in which death occurred between 1918 and 1952, form the material for the present report. In these cases *Entamoeba histolytica* was found in the liver or intestines at necropsy or in the faeces before death.

The infection was acquired in the Far East in over one-third of the cases, in the United States in a further one-third, and in other countries, including Europe, in the remainder. The onset of the disease in most cases was acute; almost four-fifths of the patients died within 6 months of the onset of symptoms, and of these 20% died within 2 weeks. Amoebiasis was correctly diagnosed in only one-third of the cases. Liver abscess was missed in one-half of the 90 cases in which the lesion was present. In 36 of these 90 cases there was a single abscess in the right lobe and in 24 there were multiple abscesses throughout both lobes. Of the remaining 30 cases, multiple abscesses were present in the right lobe in 9, a single abscess in the left lobe in 4, and a single abscess in both lobes in 3; information concerning 14 was incomplete.

The chief causes of death were intestinal perforation, uncomplicated dysentery, liver abscess without rupture, and amoebic lung abscess, in that order. Jaundice was noted in approximately 14% of cases with and without liver abscess. *C. L. Pasricha*

1142. **A Preliminary Report on the Treatment of Amoebic Dysentery with PAA-701**
A. Z. SHAFEI. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **59**, 95–99, May, 1956. 10 refs.

A trial of a new synthetic amoebicide "camoform" (diallyl-diethyl-aminomethylphenol dihydrochloride) in 15 cases of amoebic dysentery is reported from Alexandria University, Egypt. In 3 cases the condition was acute while in 12 there was a history of recurrent attacks over periods of 3 months to 5 years. Camoform was given by mouth in a dosage of 1·5 g. daily for a minimum of 12 days. Cure was obtained in 10 cases with a total dosage of 18 to 21 g., there being prompt clinical improvement with disappearance of the parasites from the stools within 9 days. In 2 cases there was a relapse, cysts of *Entamoeba histolytica* appearing in the stools, while in the remaining 3 cases the drug did not appear to have any effect.

Camoform appeared to be free from toxic side-effects; there were no alterations in the blood picture, icterus index, or erythrocyte sedimentation rate and no changes in the results of thymol turbidity and kidney function tests, or in the prothrombin time. The results are stated to show that these cases were more resistant to treatment with camoform than were those previously reported from Honduras (Hoekenga and Batterton, *Amer. J. trop. Med. Hyg.*, 1954, **3**, 849; *Abstracts of World Medicine*, 1955, **17**, 195). *R. A. Neal*

1143. **Clinical Trial of Glaucarubin in Treatment of Amebiasis**
E. C. DEL POZO and M. ALCARAZ. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 412–417, March, 1956. 6 refs.

Glaucarubin, a crystalline glycoside isolated from plants of the genus *Simarouba*, has amoebicidal properties in experimental amoebiasis. From the Instituto de Salubridad y Enfermedades Tropicales, Mexico, comes this report of the results obtained with the drug in the treatment of 78 patients with chronic amoebiasis (cystic forms of *Entamoeba histolytica* in the faeces) and 9 patients with acute amoebic dysentery (*E. histolytica* trophozoites in the faeces). At first the daily dose varied from 10 to 280 mg. and the duration of treatment from 5 to 32 consecutive days. Later it was found that an adequate response was obtained with a dosage of 3 mg. per kg. body weight per day for 5 days. Clinical improvement was evident from the first to the sixth days of treatment and no toxic symptoms were noted. There were no changes in the blood count in the 36 patients in whom this was determined before and after treatment, nor in the response to liver function tests in 10 patients.

After treatment ceased, 54 patients were observed for periods of one month to 13 months; there was a recurrence of infection in 8 of the patients with chronic amoebiasis. *C. L. Pasricha*

1144. **Treatment of Amoebiasis with "Resotren"**
L. PFANNEMUELLER. *Lancet* [*Lancet*] **1**, 934–935, June 16, 1956. 11 refs.

"Resotren", a chemical combination of chloroquine and iodohydroxyquinolone, is poorly absorbed when given by mouth and reaches the lower bowel in high concentration where about half of it is split up into its well-known amoebicidal constituents, which are absorbed. In this paper are reviewed 42 cases of amoebiasis treated with resotren at the Mosul and Hillah Hospitals, Iraq, including 31 cases of hepatitis, 6 of liver abscess, and 5 of uncomplicated dysentery. There was rapid improvement in all cases, the stools being negative for cysts and vegetative forms after treatment and remaining so for 6 months in 40 of the 42 cases. Chloroquine was

given as well as resotren for the first 2 or 3 days in the cases of liver abscess; "needling" was necessary in only one of these. Previous treatment with the broad-spectrum antibiotics had been unsuccessful in 17 cases [but the author does not indicate whether any other amoebicide had been given].

Usually a course of 40 tablets [strength not stated] was given over 12 days; if necessary, a further course of 20 tablets in 4 days was given after an interval of 8 days. The drug was well tolerated, the only side-effect being an initial diarrhoea which generally passed off in a few days.

David Friedberg

1145. **Serological Investigations in an Area of Endemic Filariasis Due to *Wuchereria bancrofti* and *Acanthocheilonema perstans* in Gambia, West Africa**
W. MINNING and J. A. MCFADZEAN. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 246–254, May, 1956. 18 refs.

In Gambia, West Africa, where filariasis due to *Wuchereria bancrofti* and *Acanthocheilonema perstans* is endemic, the complement-fixation test was carried out on specimens of serum from 247 subjects, an alcoholic extract of *Dirofilia immitis* being used as the antigen. When this antigen was tested in Hamburg on sera from 55 subjects who had never left Europe no false positive reactions were obtained. Previous work had shown that it was possible to obtain complement fixation with serum from animals, but not from man, when heavily infected with *Ascaris*. Of 51 subjects suffering from infection with *W. bancrofti*, 29 gave a positive reaction; the possible reasons for the negative reactions are discussed. Of 24 subjects harbouring microfilariae of *A. perstans*, 6 gave a positive reaction, and the same proportion of positive results was obtained in 13 subjects when both parasites were present in the blood. Of 159 subjects who lived in the endemic area but had no microfilariae in the blood, one-third gave a positive reaction; it is suggested that this was due to infection with a filaria infesting man or, less likely, cattle.

W. H. Horner Andrews

1146. **The Complement-fixation Test in Filariasis**
D. S. RIDLEY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 255–257, May, 1956. 4 refs.

In this paper from the Hospital for Tropical Diseases, London, the author analyses the results of complement-fixation tests in suspected cases of filariasis, the antigen used being an alcoholic extract of desiccated *Dirofilaria immitis*. It is pointed out that no false positive reactions were obtained with syphilitic serum. Tests were carried out on 517 specimens of serum, including sera from cases in which there was infestation with most of the pathogenic helminths. In 142 of these filariasis was diagnosed "with a high degree of probability", but confirmation by the finding of microfilariae or adult worms was possible in only 63. The failure to find microfilariae in so many cases is attributed to the short duration of infection before the test was carried out. There were only 3 cases giving a positive response to the test in which there was any real doubt about the diagnosis of filariasis. The test was most satisfactory in the diagnosis of loiasis and least satisfactory in the diagnosis of infection with *Acanthocheilonema perstans*.

The complement-fixation test is considered to be a useful supplementary aid in the diagnosis of filariasis during the first stage, when microfilariae are absent.

W. H. Horner Andrews

1147. **Leprosy: a Changing Situation in Eastern Nigeria**
T. F. DAVEY, C. M. ROSS, and B. NICHOLSON. *British Medical Journal* [*Brit. med. J.*] **2**, 65–68, July 14, 1956. 9 refs.

In recent years there has been a striking decrease in the incidence of leprosy in eastern Nigeria, and in this paper from the Nigeria Leprosy Service the reasons are discussed. Although it was recognized that cases of leprosy occurred in Nigeria and a Leprosy Ordinance was enacted in 1917, little was known of the extent of the disease in that country before 1930. In 1937 a survey by one of the present authors revealed that in an area with a total population of 14,515 the incidence of leprosy was 34 cases per 1,000 population. This survey was followed by others in which the recorded incidence was as high as 150 per 1,000. The form of leprosy encountered was relatively mild, mutilations were rare, lepromatous cases did not account for more than 10% of the total, and the response to treatment was good. In two groups of villages studied closely for more than 10 years it was found that the decrease in incidence was real—from 522 cases in 1943 to 49 in 1954 in the first of these and from 31 per 1,000 population in 1943 to 5 per 1,000 in 1951 in the second.

Discussing the causes for this phenomenal decline in the incidence of leprosy in eastern Nigeria the authors suggest that there has been a leprosy epidemic. In the early years of this century each village was an isolated unit, but with the rapid opening-up of the country infection spread, the epidemic reaching a peak about the year 1940. The decline which occurred after this time is attributed to three factors—the spread of tuberculosis, the efficacy of segregation as a control measure, and the effects of treatment. Tuberculosis is an uncommon disease in rural areas and its introduction followed the trade routes. Tuberculous infection provided some immunity against leprosy. Segregation reinforced a strong inherent taboo relating to contact with leprosy, and once segregation became the official policy it was not difficult to carry it out. By segregating the infectious cases in villages opportunities for contact diminished. Other factors influencing the decline were the wearing of clothes, with the consequent reduction in the area of skin exposed to infection, and the treatment of yaws and scabies, diseases which cause breaches in the continuity of the skin and render the subjects more susceptible to inoculation with leprosy. The authors consider, however, that the most important single cause of the decline in the incidence of leprosy is the success of treatment with the sulphone group of drugs.

William Hughes

Allergy

1148. **Adrenocortical Function in Severe Asthma.** [In English]
B. M. DAVIES. *Acta allergologica* [*Acta allerg. (Kbh.)*] **10**, 1–8, 1956. 1 fig., 12 refs.

Excretion of 17-ketosteroids is considered to be the most accurate index of adrenocortical activity. Using Norymberski's method, the author estimated the urinary excretion of 17-ketosteroids and 17-ketogenic steroids in 26 women and 10 men with severe asthma. It was found that most of the women showed no evidence of adrenal hypofunction, while in 6 of the 10 men excretion of 17-ketogenic steroids was below the lower limit of normal. There was no relationship between the severity of the symptoms and the excretion of 17-ketogenic steroids. *A. W. Frankland*

1149. **Cortisone in Treatment of Children with Chronic Asthma**
M. C. S. KENNEDY and D. C. THURSBY-PELHAM. *British Medical Journal* [*Brit. med. J.*] **1**, 1511–1515, June 30, 1956. 3 figs., 11 refs.

The effect of oral cortisone given in short courses to 12 children (9 boys and 3 girls between the ages of 9 and 15) with chronic asthma was assessed in a study reported from the North Staffordshire Royal Infirmary, Stoke-on-Trent. Half the patients were treated with cortisone and half with a placebo in a double-blind trial, those who initially received the placebo being subsequently given cortisone and vice versa. The hormone was administered in divided doses of 75 mg. daily for 3 weeks, followed by 50 mg. daily for a further 2 weeks. The results were assessed by measuring the volume of air expired in 0·75 second (the expiratory flow rate; E.F.R.) at twice-weekly attendances before and during the trial. Measurements of the E.F.R. were also made at each attendance after inhalation of an adrenaline aerosol. The E.F.R. increased in all 12 children while they were receiving cortisone, being on the average 6 litres per minute greater than the average figure while receiving the placebo, an increase of 13%. Three children showed an increase of over 20%, 2 over 10%, and the remainder less than 10%; it was considered that only those showing an increase in the E.F.R. of over 20% had derived significant benefit. Such an improvement in response to the combined effects of cortisone and adrenaline was obtained in 9 of the patients.

It appears that the beneficial effects of these two drugs is additive. The maximum improvement observed with cortisone in the dosage used was achieved only after a period of 2 to 4 weeks and was not maintained when the dose was reduced to 50 mg. daily or less. The authors stress the importance of employing an objective method of measuring ventilatory function in assessing improvement in asthma. No side-effects were observed, but long-term treatment was considered to be inadvisable in children until more is known of the effects of cortisone administered over a long period of time on the adrenal cortex. *R. S. Bruce Pearson*

1150. **Intracutaneous Asthma Vaccine Therapy in Asthmatic Children: its Application and Clinical Value**
L. TUFT and F. ERMILIO. *Journal of Pediatrics* [*J. Pediat.*] **48**, 569–580, May, 1956. 1 fig., 7 refs.

Whatever may be the mode of action of bacterial vaccines in the treatment of bronchial asthma, it has been shown that about 70% of asthmatic patients obtain benefit, but whether this benefit is due to a specific bacterial desensitization or to a non-specific protein effect is not known. Moreover, it is difficult in dealing with asthmatic children to assert that the asthma is "bacterial" or "infectious", in spite of a history of repeated colds or sinusitis, since both the "cold" and the asthma may be reactions to the same allergenic agent. Normally these vaccines, whether stock or autogenous, are given subcutaneously, but the injections may give rise to a severe and, in rare cases, even a fatal reaction.

As a result of their previous experience at Temple University Hospital, Philadelphia, with prophylactic typhoid immunization injections given intracutaneously the authors decided to employ the same route in giving a stock asthma vaccine. This vaccine was prepared from pure cultures of organisms isolated from the bronchoscopically aspirated bronchial secretions of many asthmatic patients. Treatment was usually started at the beginning of the winter, no rigid schedule being followed, but in most cases between 8 and 18 injections were given. Initially the authors used amounts of 0·1 ml., but later found that amounts of 0·01 to 0·05 ml. caused fewer local and constitutional effects. The addition of hyaluronidase did not lessen local reactions. From the results of the treatment of 125 children over some 6 years (a total of 2,036 injections) the clinical impression was gained that intracutaneous injections gave better results than the subcutaneous method and definitely reduced the number and severity of reactions. *A. W. Frankland*

1151. **Asthma and Housedust in the High Mountains**
H. A. VAN GEUNS. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **8**, 290–303, 1956. 1 fig., 19 refs.

1152. **Preparation and Properties of a Single Antigen from Giant Ragweed Pollen**
A. R. GOLDFARB, A. LIBRETTI, M. KAPLAN, H. A. ABRAMSON, and A. AARONSON. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **8**, 243–251, 1956. 4 figs., 7 refs.

Nutrition and Metabolism

1153. **Lysine and Tryptophan Content of Proteins and their Utilization for Human Growth**

A. A. ALBANESE, R. A. HIGGONS, G. M. HYDE, and L. ORTO. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 161–168, March–April, 1956. 2 figs., 18 refs.

It has been suggested that the amino-acid requirements are related to the amino-acid content of the body. The present authors, at St. Luke's Hospital, New York, and St. Luke's Convalescent Hospital, Greenwich, Connecticut, determined the nutritive value for infants of a variety of foods and related them to the ratio of lysine to tryptophan; this ratio in muscle, which represents 75% of the body protein of infants, is 6·3:1. They estimated the nutritional value of different foods—evaporated milk, casein digest, lactalbumin digest, beef muscle digest, digest of bovine plasma, and wheat gluten—from studies of nitrogen balance. The nutritional value of each of these was related to the lysine:tryptophan ratio, the nearer this ratio approached 6·3:1, the greater the nutritional value. Supplementation with lysine of those proteins with a low nutritional value and an originally low lysine:tryptophan ratio enhanced the nutritional value. For example, unsupplemented wheat gluten had a ratio of 2 and a low nutritional value; when lysine was added to give a ratio of about 6, the nutritional value approached that of milk protein. The authors suggest that these findings may have important application in the nutrition of infants in those countries where deficiency diseases such as kwashiorkor may be due to amino-acid deficiency. *John Yudkin*

1154. **Effects of Feeding Different Fats on Serum-cholesterol Level**

B. BRONTE-STEWART, A. ANTONIS, L. EALES, and J. F. BROCK. *Lancet* [*Lancet*] **1**, 521–527, April 28, 1956. 7 figs., 41 refs.

In a previous paper (*Lancet*, 1955, **2**, 1103; *Abstracts of World Medicine*, 1956, **19**, 461) the authors reported that in the multiracial community of the Cape Peninsula inter-racial differences in the incidence of coronary arterial disease were associated with parallel differences in the mean serum cholesterol level. They now report the results of a study carried out at the University of Cape Town on 6 non-European male volunteers, in each of whom the initial serum cholesterol level and fat intake were low, and on 2 European males with electrocardiographic evidence of coronary heart disease whose serum cholesterol level was initially high and who were accustomed to a high-fat diet. Two of the non-European patients were originally admitted to hospital in a scorbutic state, and 2 others with signs of vitamin-B deficiency; they were treated accordingly and continued to take vitamin supplements throughout the study. The basic diet of the 2 Europeans contained 50 g. of animal fat throughout the study, while that of the 6 non-Europeans consisted of maize-meal products and white bread supplemented by sugar and casein in order to maintain an isocaloric and isonitrogenous state; the latter diet was practically free from cholesterol and only about 3% of its caloric value was derived from fat. To the two basic diets various oils and fats were added one at a time in order to increase the proportion of calories derived from fat to 36%, 45%, and 60 to 70%.

Certain changes in the serum cholesterol level were noted which coincided with changes in the intake of fat. In 2 cases the addition of olive oil did not raise the blood cholesterol level, but with the addition of butter and beef dripping it promptly rose. The butter was then replaced by olive oil, when the serum cholesterol level fell again, even when the quantity of olive oil was doubled so that it provided 60% of the total calories. The addition of hydrogenated (hardened) ground-nut fat elevated the serum cholesterol level, which fell as soon as the non-hydrogenated natural ground-nut oil was substituted. Feeding with pilchard oil or seal oil, 100 g. daily, did not raise the serum cholesterol level—on the contrary it fell even below the level obtained with a fat-free diet. When fat equivalent in quantity to the content of 10 eggs was supplied as sunflower-seed oil the serum cholesterol level fell in spite of the simultaneous consumption of 3 g. of cholesterol and 80 g. of casein daily. After withdrawal of the sunflower-seed oil the serum cholesterol level rose again. Administration of excessive doses (1,000 mg.) of vitamin E was not associated with an immediate fall in the serum cholesterol level such as was seen when pilchard oil was given.

These results are interpreted by the authors as showing that the serum cholesterol level is affected not only by the quantity, but also by the quality of the dietary fat, the relative proportion of saturated and highly unsaturated fatty acids being the determining factor and the greater effect of animal fats being due to their higher content of saturated fatty acids. This may explain some of the discrepancies in the "dietary-fat theory" of the aetiology of coronary heart disease.

[This paper is the first in the English literature dealing with the effect of unsaturated fatty acids on the serum cholesterol level. Its importance is by no means diminished by the fact that these were only short-term experiments in which no balance studies were performed. The original paper should be consulted by all interested readers.] *Z. A. Leitner*

1155. **Some Metabolic Sequels of Gastric Surgery in Patients with and without Pyloric Stenosis**

H. E. F. DAVIES, R. P. JEPSON, and D. A. K. BLACK. *Clinical Science* [*Clin. Sci.*] **15**, 61–79, 1956. 4 figs., 9 refs.

Gastroenterology

1156. **Closing Mechanism of Lower Esophagus in Man. Radiological Study of Five Hundred Unselected Patients**
M. H. POPPEL, W. LENTINO, C. ZAINO, and H. JACOBSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 196–198, May 19, 1956. 2 figs., 14 refs.

At the Bellevue and Montefiore Hospitals, New York, the authors have examined radiologically 500 unselected patients by means of a barium-and-oil technique in an attempt to elucidate the mechanism of closure at the lower end of the oesophagus. They discuss the various previous conflicting theories which have been propounded to explain this mechanism. They could find no evidence for any "pinchcock" action of the diaphragm on the oesophagus, nor do they accept the theory that the angulation of the oesophago-gastric junction which occurs on forced respiration plays the part of a sphincter. They found that the line of junction between the oesophageal and gastric types of mucosa could often be clearly seen, and stress the fact that this line can move a considerable distance up and down the oesophagus. They are of the opinion that there is a true lower oesophageal sphincter, that it is situated between 0·5 and 3 cm. above the diaphragm, and that its site corresponds with the insertion of the elastic phreno-oesophageal membrane into the wall of the oesophagus. Above this sphincter lies the ampulla and below it the gastro-oesophageal vestibule. They state that the action of this sphincter has been mistaken for the "pinchcock" action of the diaphragm referred to, but insist that it always takes place above the diaphragm.

J. R. Belcher

1157. **Leucoplakia Buccalis and Oral Epithelial Naevi. A Clinical and Histological Study**
B. E. D. COOKE. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 151–174, May, 1956. 19 figs., 24 refs.

In this paper from Guy's Hospital, London, the author discusses the clinical and histological features of those conditions which are frequently grouped together under the title of leucoplakia buccalis because of the presence of white patches on the oral mucosa.

Altogether 36 patients were examined, and the following types of leucoplakia or, as the author prefers, keratosis, were recognized: smoker's keratosis, frictional keratosis, the leucoplakia of tertiary syphilis, and idiopathic keratosis. The lesions were considered to be due to smoking in 13 patients, 10 of whom smoked a pipe and 3 smoked cigarettes. In pipe-smokers the lesion took the form of domed papules with red centres, chiefly on the palate. The intervening mucosa was thick and white. The floor of the mouth, the tongue, and the lip might also be affected. In cigarette-smokers there was thickening of the mucosa of the cheek. Frictional keratosis was observed in 18 cases, the lesions occurring on the occlusal line of the cheeks, the commissures, the tongue, and the gingivae. Many of the patients were moderate smokers; some chewed the cheeks consciously, while others did so during sleep. The usual lesion was a bluish-white band extending the full length of the interocclusal line, though other patterns were also encountered. There were 3 cases of luetic leucoplakia in the series, a very much smaller proportion than would have been the case some 30 or more years ago. A painful tongue was the main feature in these cases. No apparent cause for the keratosis could be found in 2 cases. The lesions in these idiopathic cases tended to be diffuse and symmetrical. Finally the author describes another group of lesions termed "epithelial naevi", which were observed in 6 cases. These consisted in white patches with a regular wrinkled appearance, which tended to be symmetrical. They were sometimes present at birth or might develop later in life.

The histological appearances of the various lesions are described and illustrated and the differential diagnosis of leucoplakia, particularly from lichen planus, is discussed.

A technique for obtaining biopsy specimens of the oral mucosa is described in detail. *R. B. Lucas*

STOMACH AND DUODENUM

1158. **Influence of the Adrenal Cortex on Gastric Secretion in Man**
J. KYLE, J. S. LOGAN, D. W. NEILL, and R. B. WELBOURN. *Lancet* [*Lancet*] **1**, 664–666, May 12, 1956. 2 figs., 20 refs.

It is well known that atrophy of the gastric mucosa occurs in Simmonds's and Addison's diseases. The administration of cortisone increases gastric acidity and may cause an exacerbation of peptic ulceration; duodenal ulcer, however, has never been reported in patients with Cushing's disease. At the Royal Victoria Hospital (Queen's University), Belfast, a group of 11 patients with the latter condition was found by the fractional test-meal technique to have a high degree of gastric acidity, which was shown to be reduced postoperatively in those who underwent adrenalectomy.

The authors have therefore determined the urinary 17-hydroxycorticoid excretion in five groups of patients. Of 8 patients with Cushing's disease, 3 showed a high excretion rate; there was no significantly increased excretion in 8 normal subjects, in 8 patients with duodenal ulcer, or in 5 who had hyperchlorhydria without peptic ulceration or clinical evidence of endocrine disorder. In 5 achlorhydric patients, however, the excretion of 17-hydroxycorticoids was very low. The excretion of reducing corticoids was estimated in the 5 patients with hyperchlorhydria and was found to be high in 4 of them.

The authors suggest that adrenocortical hormones play a part in influencing the normal activity of gastric

secretion and that the gastric hypersecretion seen in Cushing's syndrome is caused by an excessive production of steroids by the adrenal cortex. *A. G. Parks*

1159. **Unconditioned and Conditioned Vascular Reactions in Patients with Peptic Ulceration in Relation to the Course of the Illness.** (Безусловные и условные сосудистые реакции у больных язвенной болезнью в связи с ее течением)
B. V. Il'inskiĭ. *Терапевтический Архив* [*Ter. Arkh.*] 28, 18–25, No. 1, 1956. 2 figs., 13 refs.

Believing that the vascular responses to various stimuli afford a means of assessing the functional state of the higher nervous centres, the author, working at the Pavlov Institute of Physiology, Leningrad, has studied these responses in 26 patients suffering from peptic ulceration and in 17 normal control subjects, the changes occurring in peripheral vessels in response to direct stimuli and conditioned reflexes being recorded plethysmographically. In the interpretation of the results, the time relationship and the degree of response to the establishment, reinforcement, and extinction of conditioned reflexes were taken into consideration.

Three types of vascular reaction have previously been defined: the labile, the inert, and the intermediate. Of the 26 patients, 9 had the labile, 8 the intermediate, and 9 the inert type of response. Of the 17 control subjects, only 4 showed the two extreme types of response. Clinically, the patients could be divided into three groups: (1) those (4 patients) whose illness was stormy and acute, with a tendency to gastro-intestinal haemorrhage and well-marked remissions and exacerbations; (2) those (8 patients) in whom the illness was of a chronic nature with little tendency to remission; (3) in the remaining 14 patients the illness had an intermediate character. Patients in Group 1 tended to have a labile type of vascular reaction, whereas those in Group 2 mainly showed an inert type of reaction. Under the influence of hospital treatment the reactions of the former tended to become more normal, but there was no alteration in those of the patients in Group 2.

The author claims that these results allow conclusions to be drawn regarding the state of excitability or depression of the cerebral cortex and subcortical formations in these patients and also regarding the relative influence of these factors on each other and on the vasomotor centres. (Illustrative recordings, together with some details of their interpretation, and a brief review of the relevant work of other authors are included in the article.)
Marcel Malden

1160. **Treatment of Chronic Duodenal Ulcer by Antroduodenectomy and *X*-irradiation. Interim Report**
G. Brown and I. J. Wood. *Lancet* [*Lancet*] 2, 169–171, July 28, 1956. 1 fig., 8 refs.

Having found that the results of treatment of duodenal ulcer by gastrectomy were disappointing in some respects, the authors subjected 142 patients with duodenal ulcer to antroduodenectomy—that is, removal of the pyloric antrum with the ulcer-bearing area of the duodenum—alimentary continuity being restored by anastomosis of the remainder of the stomach to the duodenum. In an attempt to reduce gastric secretion half of the patients were given *x*-irradiation (total tissue dose of 2,000 r) to the gastric area two months after operation. There were 3 deaths and 2 patients required gastroenterostomy to relieve stomal obstruction after operation; the remaining patients withstood the operation remarkably well.

Of 100 patients observed for periods of 12 months to 4 years, 83 had made satisfactory progress, 5 moderately good progress, and 12 had suffered from recurrent ulceration. While achlorhydria was usually observed after radiotherapy, acid secretion returned in about 18 months. The authors state that *x*-irradiation appeared to have no significant effect on results; moreover, they suggest that in view of the high rate of ulcer recurrence (12%) and the possible late effects of radiation therapy this method of treatment should be abandoned.
A. G. Parks

1161. **Gastric Diverticula.** (Дивертикулы желудка)
E. M. Kagan. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] 34, 43–49, No. 4, April, 1956. 7 figs., 15 refs.

Writing from the State Institute of Roentgenology and Radiology, Moscow, the author states that diverticula of the stomach occur more often than available literature indicates. The differential diagnosis of diverticulum from gastric ulcer and carcinoma is important and is best achieved with the help of radiography. He restricts the term diverticulum to saccular deformities of the stomach wall arising either as developmental abnormalities or due to areas of congenital localized weakness in the muscular layer. True diverticula are invariably connected with the lumen of the stomach by a neck, the radiological demonstration of which is important in diagnosis, and in uncomplicated cases their outline is regular, but inflammatory changes may lead to deformity of the outline. The typical site of origin is on the posterior wall of the cardiac portion of the stomach. The size may vary from that of a small pea to that of a small tangerine orange. The symptoms are very variable, many diseases of the gastro-intestinal tract, including the gall-bladder, being simulated. Occasionally they are symptomless. In radiographical diagnosis multiaxial views in the horizontal position are essential, films being exposed before, during, and after the ingestion of barium. *A. Swan*

1162. **Carcinoma of Stomach in Relation to ABO Blood-groups**
D. Jennings, R. H. Balme, and J. E. Richardson. *Lancet* [*Lancet*] 2, 11–12, July 7, 1956. 3 refs.

The blood groups of, and tumour sites in, 119 patients with gastric carcinoma operated on at the London Hospital during the 5-year period 1949–53 have been analysed. Among patients with carcinoma originating in the pylorus and antrum there were more with blood of Group A (42) than with blood of Group O (20). No such excess of patients with blood of Group A was observed when the growth originated elsewhere in the stomach. Thus there is no support for the hypothesis

of Køster *et al.* (*Lancet*, 1955, **2**, 52; *Abstracts of World Medicine*, 1956, **19**, 117) that blood of Group A is associated with mucosal atrophy and achlorhydria. The present authors suggest that in Group-A patients the antral and pyloric mucosa is more frequently inflamed and that gastritis predisposes to both simple ulceration and carcinoma. *A. Wynn Williams*

LIVER

1163. **Chronic Constrictive Perihepatitis, a Special Form of Curschmann's "Sugar-icing Liver". A Preliminary Attempt at Surgical Treatment.** (La périhépatite constrictive chronique (forme particulière de foie glacé de Curschmann). Premier essai d'une thérapeutique chirurgicale directe)

A. Lemaire, E. Housset, J. Natali, and J. P. Etienne. *Presse médicale* [*Presse méd.*] **64**, 943–946, May 23, 1956. 8 figs., 18 refs.

The condition of constrictive thickening of the capsule of the liver of unknown aetiology ("sugar-icing" liver) has been known since the middle of the 19th century. In the opinion of Pick (1896) it was usually or even always a result of, or associated with, chronic pericarditis or pleuritis, but recent work has disproved this, although the condition is often associated with an enlarged spleen and perisplenitis. The perihepatitis may lead to portal hypertension, sometimes with ascites and oesophageal varices, despite a fairly normal liver function. On the other hand, it may accompany alcoholic or other forms of hepatic cirrhosis.

In this paper the authors describe 2 cases, one of each type. The first patient, a man aged 38, had a 4-year history of increasing disability from ascites, requiring ever more frequent paracentesis; there was no history of alcoholism. The diagnosis was established by needle biopsy, peritoneoscopy, and the finding of almost normal liver function as determined by the usual tests. At exploratory laparotomy thickening of the capsule was found on both surfaces of the liver, almost completely encasing the organ, only the hilum being free. Portal tension was high (35 cm. of water). At operation much of the thickened material was stripped off the superior and inferior surfaces of the liver, whereupon the portal venous pressure fell almost at once to 24 cm. H_2O. For some time after the operation the ascites continued to recur, although in gradually decreasing amounts. Definite improvement began 3 months later and the portal pressure remained low; 6 months after operation the monthly volume of fluid aspirated was reduced to one-quarter of the preoperative amount, and the patient's general condition was good. The second patient, a man of 46, was admitted to hospital with haematemesis, jaundice, and impending coma. In spite of treatment this patient died of a profuse haematemesis 48 hours after admission. Necropsy revealed perihepatitis of the convex border of the liver and typical multilobular cirrhosis. It was found that the thickened capsule could be stripped off the liver like the peel off an orange.

In a footnote to their paper the authors mention a third case, very similar to the first, in which the operation of perihepatectomy (carried out in April, 1956) was well tolerated. Discussing the aetiology of the condition, which is still obscure, they suggest that some cases of cirrhosis of the liver may result solely from such perihepatic constriction and that in these cases operation may have good results. *Norman C. Tanner*

1164. **Effect of Venous-shunt Surgery on Liver Function in Patients with Portal Hypertension. A Follow-up Study of 125 Patients Operated on in the Last Ten Years**

D. S. Ellis, R. R. Linton, and C. M. Jones. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 931–936, May 17, 1956. 6 figs., 10 refs.

The authors describe the results of a follow-up study of 125 patients with portal hypertension who have undergone 130 shunt operations at the Massachusetts General Hospital, Boston, during the last 10 years. All had demonstrable oesophageal varices and all had been followed up for at least 12 months. Splenectomy and spleno-renal anastomosis were performed on 88 patients, of whom 21 (24%) eventually died, 10 (11%) of them from liver failure; direct porta-caval anastomosis was performed on 37 patients, of whom 15 (40·5%) eventually died, 10 (27%) of liver failure. In view of the difference in these mortality figures the authors now prefer to perform splenectomy and spleno-renal anastomosis, despite the more frequent recurrence of bleeding following this operation.

Wedge biopsy of the liver was performed at each operation and revealed the presence of a normal liver in 20 cases, portal cirrhosis in 98 (20 alcoholic, 31 postnecrotic, and 47 unclassified), biliary cirrhosis in 4, and a condition classified as "hepatitis" in 3. There were 14 operative deaths and 23 patients died subsequently (12 from liver failure and 2 from oesophageal bleeding), giving an over-all mortality of 29% over 10 years. Of the patients with a normal liver, 16% died, none from liver failure, while in the alcoholic cirrhotic group the mortality was 50%, among those with postnecrotic cirrhosis 32%, and those with biliary or unclassified cirrhosis 25%.

In all, 111 patients (89%) survived operation, 102 of these (81%) surviving for at least one year, compared with a reported survival rate of 30% in those not operated on after bleeding. Of 54 patients operated on at least 5 years previously, 27 (50%) are still living, compared with a 5-year survival rate of 20% among patients not operated on after variceal bleeding. Recurrence of oesophageal bleeding after operation was twice as common (26%) in those with a normal liver as in those with cirrhosis; in the latter group haemorrhage occurred in 17% of those treated by spleno-renal shunt, compared with 3% of those treated by porta-caval shunt. After both operations there was a marked reduction or disappearance of the varices in over 80% of cases, although this sometimes took many months.

Liver function was investigated in 82 of the survivors, of whom only 15 were incapacitated to some degree by disturbed liver function. Changes in the serum albumin and bilirubin levels and the results of cephalin flocculation and "bromsulphalein" retention tests showed

no correlation with the clinical assessment. Venous-shunt surgery did not appear to lead to more impairment of liver function than would be expected in patients with portal hypertension. The authors consider that surgery will relieve portal hypertension, reduce the incidence of bleeding from oesophageal varices, significantly lengthen the survival time, and improve the general state of health. *A. G. Shaper*

LARGE INTESTINE

1165 (*a*). **Biopsy Studies in Ulcerative Colitis**
S. C. TRUELOVE and W. C. D. RICHARDS. *British Medical Journal* [*Brit. med. J.*] **1**, 1315–1318, June 9, 1956. 7 figs., 6 refs.

1165 (*b*). **Abnormal Epithelial Cells in Ulcerative Colitis**
M. M. BODDINGTON and S. C. TRUELOVE. *British Medical Journal* [*Brit. med. J.*] **1**, 1318–1321, June 9, 1956. 8 figs., 13 refs.

The first of these two papers from the Radcliffe Infirmary, Oxford, describes a study of the histological material obtained by biopsy of the rectal mucosa of patients with ulcerative colitis; the method and the instrument used, which is similar in principle to the Woods gastric biopsy tube, have already been described (*Brit. med. J.*, 1955, **2**, 1950; *Abstracts of World Medicine*, 1956, **19**, 447).

The 11 biopsy specimens from 42 patients showed inflammatory infiltration of the lamina propria with plasma cells and lymphocytes. Eosinophil and neutrophil granulocytes were numerous in the vicinity of crypt abscesses. The histological assessment was made without clinical knowledge of the cases. In a control group of 24 patients with nervous diarrhoea and other disorders the biopsy specimens from all but 2 of them showed normal histological appearances. In 67 out of 71 specimens from patients with active ulcerative colitis evidence of inflammation was present, while more than half of 40 specimens obtained from patients in remission also showed inflammation. The authors suggest that this finding of inflammatory damage in apparently normal or healed mucosa may be of value in detecting very early cases of ulcerative colitis, and also in distinguishing the disease from other types of chronic diarrhoea, as well as giving some guidance as to the prognosis in apparently cured patients. In 2 of their patients histological relapse preceded clinical relapse by several weeks.

The second paper describes the abnormal cells found in smears of the rectal mucosa obtained with a special perspex tool (illustrated) and stained by Papanicolaou's method. In about two-thirds of 94 smears from patients with ulcerative colitis abnormal epithelial cells were observed. These cells had large nuclei with a disturbed chromatin pattern, the nucleus in extreme cases being five times the diameter of that of a normal epithelial cell. There was good correlation between the incidence of these abnormal cells and the severity of the disease, but none with the duration of the disease. It is pointed out that the abnormal cells had many of the features of malignant cells, but they may also represent the result of an arrest of maturation in the development of differentiated colonic epithelium. Other possibilities discussed are that the cells represent an attempt at regenerative repair, or that the abnormality is due to toxic effects on normal epithelial cells. *John Naish*

1166. **ACTH and Cortisone Therapy in Ulcerative Colitis**
A. RICHMAN, I. STERNLIEB, and A. WINKELSTEIN. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **1**, 206–214, May, 1956. 24 refs.

The results obtained with ACTH and cortisone in the treatment of 27 cases of ulcerative colitis are discussed, these cases representing about one-third of the total number of such cases seen at the Mount Sinai Hospital, New York, from 1952 to 1954. The majority of the patients were severely ill and had failed to respond to the usual supportive medical treatment. Extremely ill patients received initially 40 to 100 units of ACTH daily by intravenous injection, or 100 mg. of hydrocortisone daily by the same route, or multiple doses of aqueous ACTH (80 to 100 units daily) by intramuscular injection. After 7 to 27 days treatment was changed, most of the patients receiving instead either 80 to 100 units a day of ACTH gel by intramuscular injection or cortisone by mouth in a daily dosage of 30 to 50 mg.—the same regimen of treatment as the less severely ill patients received from the start.

The authors were unable to detect any difference between the results achieved with ACTH and those achieved with cortisone. In the extracolonic manifestations of the disease there was a uniformly good and often prompt response to any form of treatment. Of 6 cases of acute ulcerative colitis there was a remission in 3 and temporary improvement in one, the condition remaining unchanged or becoming worse in 2. Assessing the results in chronic ulcerative colitis on the basis of hospital admission (28 in 21 patients) the authors found as follows: of 16 instances of moderately severe disease remission was obtained in 13 and temporary improvement in 3; of 9 instances of severe disease remission was obtained in 4, temporary improvement in 2, while in 3 the condition was unchanged or worse; and of 3 instances of very severe disease remission was achieved in one, while in 2 the condition became worse.

The common side-reactions of steroid therapy were observed in 11 cases, but none was severe enough to call for cessation of treatment. Perforation of the colon occurred in 2 very ill patients, and postoperative shock, due to adrenal exhaustion, in one patient treated with ACTH. In one case there was haemorrhage 8 days after the last dose of ACTH. Operation was ultimately necessary in 9 cases in the series, and the authors consider that the preliminary steroid therapy achieved a remission or some improvement in general health which reduced the risks of operation. Altogether 20 of the 27 patients improved with steroid therapy, and of these 11 remained well for 2 to 18 months, 6 relapsed 4½ to 14 months after discharge, and 3 were untraced. The mechanism whereby the improvement was achieved is not known. *A. Gordon Beckett*

Cardiovascular System

1167. **Observations on the Individual Effects of Smoking on the Blood Pressure, Heart Rate, Stroke Volume and Cardiac Output of Healthy Young Adults**

C. B. THOMAS, J. L. BATEMAN, and E. F. LINDBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 874–892, May, 1956. 5 figs., 38 refs.

In this paper the authors report a study of the circulatory effects of smoking cigarettes in 113 healthy medical students. The systolic and diastolic blood pressures were recorded, as were the heart rate, stroke volume, cardiac output, and cardiac index, before and after smoking one and two cigarettes. While statistically significant changes occurred in all these values, there was no constant pattern. However, the authors observed several subgroups of individuals with similar characteristics of change in the circulatory patterns, and a correlation was found with family history. In subjects whose parents were hypertensive and whose cardiac output and cardiac index before smoking were large the increase in these values after smoking was twice as high as in subjects with healthy parents. Very little increase in cardiac output and cardiac index was found in subjects whose parents had coronary arterial disease, in contrast to the findings in subjects with healthy parents. *J. Warwick Buckler*

1168. **Effects of Squatting on the Normal and Failing Circulation**

E. P. SHARPEY-SCHAFER. *British Medical Journal* [*Brit. med. J.*] **1**, 1072–1074, May 12, 1956. 4 figs., 8 refs.

The response of the circulation to the increase in the filling pressure of the right heart caused by squatting was studied at St. Thomas's Hospital, London, in 26 healthy subjects and 16 patients with varying degrees of heart failure. The subjects squatted with their weight resting on their heels, and arterial pressure, right heart filling pressure, and forearm blood flow were measured. In healthy persons the stroke output and pulse pressure increased on squatting; a rise in the forearm blood flow was then associated with a reduction in the increased pressure. When the subject resumed the standing position a transitory fall in arterial pressure was observed. In heart failure there was a slight increase in blood pressure, but no change in pulse pressure or forearm blood flow. When heart failure was severe arterial pressure increased on squatting, but the pulse pressure decreased, indicating a smaller stroke volume.

The results are interpreted as indicating that it is pulse pressure rather than mean arterial pressure which determines the general vasomotor tone. In severe cardiac failure a rise in the mean arterial pressure precedes the decrease in pulse pressure, and the author suggests that there is some initiator of vasoconstriction other than the baroceptor mechanism. He also suggests that such a reflex may originate in the low-pressure system of the left atrium. *H. E. Holling*

1169. **Effect of Molar Sodium Lactate in Increasing Cardiac Rhythmicity. Clinical and Experimental Study of Its Use in the Treatment of Patients with Slow Heart Rates, Stokes–Adams Syndrome, and Episodes of Cardiac Arrest**

S. BELLET, F. WASSERMAN, and J. I. BRODY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1293–1298, April 14, 1956. 6 figs., 12 refs.

The authors, from the General Hospital and the Graduate Hospital of the University of Pennsylvania, Philadelphia, describe the effect of intravenous and intracardiac injections of molar sodium lactate on 5 healthy controls and 41 patients with a slow heart rate, the factors studied including the electrocardiogram and blood electrolyte values, *p*H, and CO_2-combining power as well as the clinical response. In 3 patients with sinus bradycardia there was an increase in heart rate of 50 to 75% above control values during the intravenous infusion of 100 to 160 ml. of molar sodium lactate over 10 to 15 minutes. The same dose given by the same route increased the heart rate in 5 out of 6 patients with partial A-V block and 10 out of 12 with complete A-V block. From a study of 4 cases in which there were Stokes–Adams seizures the authors suggest that the prompt intravenous administration of 20 to 80 ml. of this preparation over a period of 2 minutes, followed by an intravenous infusion at the rate of 1 ml. per minute for 6 to 12 hours, may suffice to prevent subsequent attacks. In 12 cases of terminal cardiac arrest the heart beat was restored by intravenous or intracardiac injection, within 2 minutes, of molar sodium lactate, and was maintained, with associated artificial respiration, for as long as 9 hours by continuous infusion of the drug.

There were few toxic effects from the sodium lactate injections. Pulmonary oedema was not encountered but extrasystoles occurred in 4 cases. The blood pressure, when low, was sometimes restored to normal. It is considered that the mode of action of the lactate is related to the alkalosis produced by the injection, and that the lactate is metabolized.

W. J. H. Butterfield

1170. **Diagnosis and Treatment of Cardiac Pericarditis by Pericardial Biopsy**

W. L. PROUDFIT and D. B. EFFLER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 188–192, May 19, 1956. 3 figs., 7 refs.

The authors describe a technique whereby small pieces of pericardium can be taken for biopsy and at the same time drainage of the pericardial sac into the more absorbent pleura can be established. This procedure has been carried out at the Cleveland Clinic Foundation on 16 patients. In only one instance, a case of tuberculous pericarditis, were acid-fast bacilli isolated, and in one *Streptococcus viridans;* in 11 cases the cultures were sterile [so that in fact the investigation yielded but

little information]. There were 5 cases of haemorrhagic effusion in the series, but the aetiology of this condition was not established.

[The authors present little evidence to suggest that the method has any advantages over a more conservative technique.] *J. R. Belcher*

1171. **Clinical Features and Diagnosis of So-called Idiopathic Isolated Myocarditis.** (К клинике и диагностике так называемого идиопатического изолированного миокардита)

M. I. Teodori. *Терапевтический Архив* [*Ter. Arkh.*] 28, 36–45, No. 3, 1956. 9 figs., 18 refs.

Present-day views on the condition known as idiopathic isolated myocarditis—a diffuse interstitial myocarditis with destructive dystrophic changes in the muscle fibres and involvement of the small arteries and arterioles—are discussed and 2 cases, one diagnosed and the other suspected during life, are described at length.

The clinical and diagnostic points made are as follows. The rapid development and steady increase of cardiac insufficiency in the absence of previous valvular, coronary arterial, or hypertensive disease are suggestive. In the initial stages symptoms of left ventricular insufficiency will depend on the progress of the disease. There is acute enlargement of all parts of the heart, presenting a radiological picture resembling that of cor bovinum. There is definite and fairly constant disturbance of conduction and cardiac rhythm, resulting in polytopic extrasystoles and intermittent arrhythmias. Multiple emboli in both the systemic and pulmonary circulations result from intracardiac mural thrombi, and these determine the pleomorphism of the clinical picture, which may simulate conditions in which there is general vascular involvement, for example, disseminated angiitis. While pathogenetically the condition may be allergically determined, the aetiology still remains obscure.

R. Crawford

CONGENITAL HEART DISEASE

1172. **Haematogenous Brain Abscess in Cyanotic Congenital Heart Disease**

E. J. Newton. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 201–220, April, 1956. 7 figs., bibliography.

Over the 10-year period 1944–53 69 patients with solitary haematogenous brain abscess have been treated at the United Birmingham Hospitals; of these, 7 had congenital heart disease of the cyanotic variety, that is, with a central venous-arterial shunt. These cases were specially investigated, are described in detail, and discussed together with 72 previously reported cases from the literature, the salient features of which are given in a table.

In most of these 79 cases the abscess arose without any underlying septicaemia or pyaemia and in the absence of subacute bacterial endocarditis, nor could it be attributed to any thoracic cause such as lung abscess, empyema, or bronchiectasis, or to infection of the mastoid or paranasal air sinuses—in short, to none of the usual causes of brain abscess. It appears, therefore, that a central venous-arterial shunt predisposes to haematogenous brain abscess, possibly on account of the partial by-passing of the pulmonary capillaries, where it is probable that many blood-borne bacteria are filtered out of the circulation and dealt with effectively in the normal person during the course of a transient bacteriaemia. The author stresses the importance of being aware of the tendency for brain abscess formation in cases of cardiac malformation of this type; in cases with an arterio-venous shunt there appears to be no special association with brain abscess.

Of 75 of the 79 cases reviewed, 40 were in males and 35 in females, so that the sex distribution was approximately equal. The patients' ages ranged from 3 to 57 years, average 16·3 years, the highest incidence (23 cases) being in the age group 5–9. The most frequent type of cardiac malformation was Fallot's tetralogy (23 certain cases and 12 probable cases). There appeared to be no special site of predilection for the abscess in the brain. The diagnosis of the condition lies largely in being aware of its possibility; the most prominent symptom in these cases was prolonged headache. Treatment, by aspiration through a burr-hole and systemic administration and local injection of an antibiotic, was on orthodox lines.

G. S. Crockett

1173. **Cardiac Septal Defects. I. Ventricular Septal Defect. Analysis of One Hundred Cases Studied during Life**

D. F. Downing and H. Goldberg. *Diseases of the Chest* [*Dis. Chest*] **29**, 475–491, May, 1956. 2 figs., 6 refs.

The authors believe that most textbook descriptions of ventricular septal defects wrongly convey the impression that these lesions are relatively benign. They have therefore analysed the records of 100 patients (50 of each sex) with such a lesion seen at Hahnemann Medical College Hospital and the Bailey Thoracic Clinic, Philadelphia, of whom 76 were under 15 years of age. In 4 cases there was a family history of congenital heart disease, while of the 76 for whom an adequate history was available, 24 (31·4%) had near relatives suffering from diabetes. All the patients were studied by means of cardiac catheterization, and in 22 cases angiocardiography or thoracic aortography was carried out in addition.

Symptoms possibly of cardiac origin were present in 89 patients, the chief being fatigue in 72, dyspnoea in 71, and cyanosis in 39, while cardiac failure had occurred in 22; rarer symptoms were chest pain, chronic cough, paroxysmal tachycardia, haemoptysis, and syncope. In 33 cases pneumonia or other severe respiratory infection had occurred at least once, an incidence not significantly different, however, from that (26 cases) among 100 patients with pulmonary stenosis. The most common physical sign was a systolic murmur along the left sternal border. Radiologically, the great majority of patients showed right ventricular enlargement with exaggeration of the hilar and peripheral pulmonary vessels. Evidence of right ventricular hypertrophy was found in 59% of the electrocardiograms. Cardiac cathe-

terization revealed a rise in the oxygen content of the blood on passing from right auricle to ventricle in 90 patients, and 34 were thought to have had a right-to-left shunt. The volume of the shunt and total pulmonary resistance were calculated in a number of patients; 72 patients were found to have pulmonary hypertension, although the pulmonary venous capillary and systemic blood pressures were normal in all cases.

As in other conditions causing a left-to-right shunt, the pulmonary vascular resistance in cases of ventricular septal defect increases, probably as a result of vascular constriction, and later intimal and medial thickening occurs. Thus there is a progressive elevation of right heart pressure; when this exceeds the systemic pressure a right-to-left shunt with cyanosis develops. In this way the features of Eisenmenger's complex appear. The authors do not consider this complex to be a separate entity; their findings suggest that in all cases the aorta can be " aligned " with the left ventricle, and that true overriding in this condition does not occur. They stress the importance of cardiac catheterization in the diagnosis of ventricular septal defect and discuss the possible findings and certain pitfalls in the procedure. In conclusion they emphasize that ventricular septal defect is a serious lesion, which causes symptoms in the majority of those affected and cardiac failure in a large number.

F. Starer

1174. **Cardiac Septal Defects. II. Atrial Septal Defect. Analysis of One Hundred Cases Studied during Life**

D. F. Downing and H. Goldberg. *Diseases of the Chest* [*Dis. Chest*] **29**, 492–507, May, 1956. 1 fig., 4 refs.

In this further study [see Abstract 1173] the authors analysed the records of 100 patients suffering from atrial septal defect without significant complications. Of these patients 72 were female and the majority were over 15 years of age. No significant history of a difficult pregnancy was obtained, but a family history of heart disease was elicited in 5 cases, and close relatives of 20% of the patients suffered from diabetes.

The commonest symptoms were dyspnoea, fatigue, chest pain, and paroxysmal tachycardia. Cardiac failure occurred in 43 patients, subacute bacterial endocarditis in 3, and cerebral vascular accidents in 4. Of 47 pregnancies in 24 women, 30 went to term normally. The commonest auscultatory finding (92 cases) was a systolic murmur, usually along the left sternal border; a diastolic murmur was present in addition in 28 patients, while in 4 there was no murmur. Other common signs were an accentuated second pulmonary sound, cardiac enlargement, a systolic thrill at the apex, and deformity of the thorax. The electrocardiogram showed evidence of right ventricular hypertrophy in 58 cases, while in only 21 was there right bundle-branch block and in 10 atrioventricular block. In 83 there was radiological evidence of cardiac enlargement, the right ventricle being involved in 79. The pulmonary arteries were enlarged and pulmonary vascular markings increased in 80 cases, while pulmonary hypertension, as revealed by cardiac catheterization was present in 65.

The authors assert that there is no real evidence for an increased incidence of rheumatic fever in patients with atrial septal defect. On the other hand they suggest that many episodes of heart failure are misdiagnosed as pneumonia. Catheterization studies showed that larger shunts were present in atrial than in ventricular septal defect, while pulmonary arterial pressure tended to be lower. Pulmonary blood flow was also less than in ventricular septal defect, and pulmonary vascular sclerosis tended to be delayed, probably owing to the limitations on pulmonary blood flow imposed by a normal right ventricle.

It is suggested that treatment is most likely to be successful in patients with a marked left-to-right shunt. Little is to be hoped for when there is no shunt, and indeed closure of the defect when the flow is from right to left may increase the burden on the right atrium. These points are discussed in some detail.

F. Starer

1175. **Dilatation of the Pulmonary Artery in Pulmonary Stenosis**

F. S. P. van Buchem. *Circulation* [*Circulation* (*N.Y.*)] **13**, 719–724, May, 1956. 10 figs., 9 refs.

An attempt was made at the University of Groningen to correlate the diameter of the pulmonary artery (obtained at angiography with the patient in the oblique position) and the systolic pressure difference between the right ventricle and pulmonary artery in 20 cases of simple pulmonary valvular stenosis. Stenosis was mild in the majority, the pressure difference being under 30 mm. Hg in 10, 40 to 50 mm. Hg in 6, and over 100 mm. Hg in 4. The diameter of the pulmonary artery, normally 22 to 33 mm. by this method, ranged from 30 to 75 mm., and evidently bore no relation to the severity of the stenosis or to the age of the patient. In 6 cases of " idiopathic dilatation of the pulmonary artery " in which pulmonary stenosis had been excluded by cardiac catheterization the appearance of the dilated artery resembled that found in cases of pulmonary stenosis and its diameter ranged from 39 to 49 mm. From this evidence the author concludes that dilatation of the pulmonary artery is probably a primary condition, and is not merely secondary to the valvular stenosis.

J. A. Cosh

1176. **Pulmonary Valvular Stenosis with Intact Ventricular Septum. Results of the Brock Type Valvulotomy**

C. W. Lillehei, P. Winchell, P. Adams, I. Baronofsky, F. Adams, and R. L. Varco. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 756–759, May, 1956. 2 refs.

The authors of this paper from the University of Minnesota Hospitals, Minneapolis, report the findings on re-examination after operation of 20 out of 43 patients subjected to pulmonary valvotomy by the Brock technique, the average interval since operation being 15 months. The auscultatory findings changed very little, the systolic murmur and thrill remaining after valvotomy. In a small number of cases there was a diastolic murmur consistent with pulmonary incompetence. The most significant alteration occurred in the right ventricular

pressure. For the whole group the average reading was 116 mm. Hg before operation and 56 mm. Hg afterwards; when the 5 cases in which there was no significant alteration were excluded the figures were 123 and 43 mm. Hg respectively. Two explanations are offered for the failure in these 5 cases: (1) simple dilatation only was accomplished—the valvulotome did not incise the valve; and (2) infundibular stenosis was unrecognized despite attempts to exclude it. In these cases pressure was not recorded at operation, as recommended by Brock, so that the situation could not be corrected at the time. Especially gratifying was the response in the cyanotic group (7 patients), in whom the fall in the haemoglobin level and the increase in arterial oxygen saturation reflected the significant alteration produced in the right ventricular pressure. *R. G. Rushworth*

CHRONIC VALVULAR DISEASE

1177. **Clinical and Hemodynamic Studies of Tricuspid Stenosis**

P. N. Yu, D. E. Harken, F. W. Lovejoy, R. E. Nye, and E. B. Mahoney. *Circulation* [*Circulation (N.Y.)*] 13, 680–691, May, 1956. 9 figs., 11 refs.

A special study is reported of 5 cases of tricuspid stenosis accompanying mitral stenosis, these having been found during investigation over a recent 3-year period of 100 cases of mitral stenosis. Characteristic symptoms were dyspnoea on effort, engorgement of the neck veins, not necessarily with oedema, visible "a" waves in the neck veins of the 3 patients who were in sinus rhythm, and cyanosis. In all the cases there was a rumbling diastolic murmur in the tricuspid area, intensified on inspiration, and the right atrial pressure was raised, the pressure difference in diastole between the atrium and ventricle ranging from 4 to 16 mm. Hg and tending to increase with effort. Atrial systole caused pressure waves up to 18 mm. Hg. In 3 patients there was an unexplained rise in the end-diastolic pressure in the right ventricle. Resting pulmonary arterial pressure was only slightly raised and the cardiac output was low.

One patient refused operation and died 13 months after she was first seen. Tricuspid valvuloplasty was performed in 4 cases, with concomitant mitral surgery in 3 of them. In 2 cases re-examined after operation the right atrial pressure and the pressure difference across the tricuspid valve had fallen. *J. A. Cosh*

1178. **Tricuspid Stenosis in Rheumatic Heart Disease.** (Les rétrécissements tricuspidiens rhumatismaux).

P. Soulié, J. Carlotti, F. Joly, J. Forman, and H. Jallut. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **1**, 554–574, May, 1956. 4 figs., 36 refs.

The authors describe a study of 31 female and 2 male patients with functional stenosis of the tricuspid valve of rheumatic origin who were treated at the Hôpital Lariboisière, Paris. In 15 cases the diagnosis was confirmed at operation or post-mortem examination, but anatomical confirmation of the lesion was not possible in the remaining 18. Operation to relieve the stenosis was performed in 4 cases, in all of which mitral stenosis was also present and was dealt with at the same time. Haemodynamic studies suggested the presence of tricuspid stenosis in the others.

Tricuspid stenosis may be diagnosed by cardiac catheterization before the classic signs of the condition appear. The coexistence of tricuspid stenosis in a patient with mitral stenosis may be suspected if the second pulmonary sound is not increased and if there are signs in the aortic area. In addition, radiography may show marked enlargement of the heart to the right and an absence of pulmonary congestion. Minimal right axis deviation may be found in the electrocardiogram, occasionally accompanied by right bundle-branch block, but no evidence of right ventricular hypertrophy. At cardiac catheterization tricuspid stenosis is diagnosed by an increase in the right atrial diastolic pressure and a pressure gradient across the tricuspid valve; in some cases exercise may be required to demonstrate this change. The pulmonary vascular pressures are usually lower than would be expected from the degree of mitral stenosis, unless the tricuspid valve is incompetent as well as stenosed. The cardiac output is reduced.

In 3 of the present cases a successful tricuspid valvotomy was performed and 7 other cases have been reported in the literature; the operation appears to be a useful one. *H. E. Holling*

1179. **A Medical Appraisal of Transaortic Commissurotomy**

J. F. Uricchio, R. Litwak, C. Denton, H. Goldberg, and W. Likoff. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 844–860, May, 1956. 3 figs., 6 refs.

The surgical approach to the stenosed aortic valve may be from below, through the left ventricle, or from above, through the aorta. The latter route, in which an artificial pouch is used, permits direct digital palpation of the valve; it was hoped that the risks of ventricular fibrillation and of aortic regurgitation would be less with this method than with transventricular commissurotomy, but this has not been fulfilled. In this paper from Hahnemann Medical College and Hospital and the Bailey Thoracic Clinic, Philadelphia, the results of transaortic commissurotomy in 40 cases are analysed. There were 4 operative deaths, 2 from ventricular fibrillation, one from cerebral embolism, and one from rupture of a cusp. The ages of the patients, 34 men and 6 women, ranged from 25 to 60 years, and 18 of them had aortic regurgitation as well as stenosis. The common symptoms in order of frequency were dyspnoea, fatigue, angina, vertigo, and syncope. Regular rhythm, a loud, rough, systolic murmur, and a thrill were present in all cases. The left heart was usually enlarged in the radiograph and abnormalities were observed in the electrocardiogram.

Complications, which were frequent in the survivors, included atrial fibrillation, heart failure, and subacute bacterial endocarditis, the last-named being responsible for 4 of the 6 deaths which occurred after the patients had been discharged from hospital. The cause of 2 late

deaths was not determined. It is suggested that the infection may have been related to the use of the ungloved finger or to inadequate antibiotic cover. Aortic regurgitation developed in 2 cases. Murmurs were frequently altered, and there was often improvement in the brachial arterial tracing. The assessment of results was limited to the 27 patients operated on at least 3 months previously, including the 6 who died after discharge. Of the 21 survivors, 15 were improved, 4 were worse, and in 2 the condition was unchanged. Angina consistently disappeared.

From the results the authors consider that surgical treatment can be equally effective by either route, and that success depends largely on the original state of the valve. Contraindications to operation include other incorrectable valve lesions, persistent cardiac failure, rheumatic activity, and bacterial endocarditis. As an aid to the selection of patients for operation the following grouping is suggested: Grade 1, a murmur only; Grade 2, no symptoms, but left ventricular enlargement or strain present; Grade 3, dyspnoea, angina, or syncope accompanied by left ventricular enlargement; and Grade 4, advanced manifestations of aortic stenosis and heart failure. Operation is indicated in patients with Grade-2 or Grade-3 disability. Operation in patients included in Grade 4 carries a high risk and may not be successful. *M. Meredith Brown*

1180. **The Surgical Treatment of Aortic Stenosis**
C. P. Bailey, H. E. Bolton, H. T. Nichols, W. L. Jamison, and R. S. Litwak. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 375–437, April, 1956. 30 figs., 42 refs.

[This article is probably the most comprehensive and detailed account of the surgical treatment of aortic stenosis that has been written. Moreover, the authors do not confine themselves to surgery but give an extensive survey of the aetiology and haemodynamics of the condition.]

In this review, from Hahnemann Medical College and the Bailey Thoracic Clinic, Philadelphia, of the surgical treatment of aortic stenosis, three main types are distinguished. (1) A congenital form, in which the valves are often bicuspid and post-stenotic dilatation is usually present; with this type coarctation of the aorta may be associated. (2) Arteriosclerotic stenosis; this type is probably less common than is often supposed and many of the cases regarded as arteriosclerotic are actually of rheumatic origin. (3) Rheumatic aortic stenosis; this form is very similar in pathology to mitral stenosis, the vegetations producing thickening and fusion of the edges of the cusps and leaving a more or less central opening which is triradiate. In all three types the walls of the left ventricle steadily hypertrophy as the stenosis develops, but the chamber itself does not dilate until hypertrophy has reached its limit. The fact that the thickened muscle is unduly irritable and soft makes its manipulation difficult. The critical point at which there is difficulty in ejection of blood from the ventricle occurs when the area of the orifice is reduced by 75 to 90%. The period of ejection is then unduly prolonged, as may be shown by a study of pressure curves. The blood supply to the heart muscle is also diminished as a result of the lower systolic pressure at the root of the aorta, thus accounting for the anginal symptoms from which many patients suffer.

Clinically, the early symptoms consist of lassitude and fatigue, followed later by shortness of breath on exertion and orthopnoea. Dizziness and fainting are common and anginal attacks occur on slight effort. The characteristic murmur is a short, harsh, systolic one heard over the aortic area and conducted up the carotid arteries or in some cases towards the apex. Fibrillation is rare, and when it does occur the coexistence of a mitral lesion should be suspected. The blood pressure is usually within normal limits, though it is said to be low in systole and high in diastole. The coexistence of mitral stenosis with the aortic lesion is common (44% of cases in the authors' series). On the other hand mitral insufficiency is rare (6% of cases) and is then probably due to dilatation of the mitral ring. The possibility of the tricuspid valve being also involved is appreciable (17%), and this was the predominant lesion in some 11% of cases. The pulmonary valve is rarely affected. The necessity of recognizing stenosis in other valves is important, because if only one source of obstruction is removed the circulatory position is made worse at a later date.

The surgical approach to the aortic valve may be through the left ventricular wall or through the aorta. The transventricular approach in 68 cases of uncomplicated aortic stenosis gave an operative mortality of 28%. In 87 cases of combined mitral and aortic stenosis the mortality was 18%. The causes of operative death are principally ventricular fibrillation, heart arrest, and haemorrhage. The transaortic approach is now considered to be safer. Control of haemorrhage through the incision in the aorta is effected by using a pouch or pocket of pericardium or plastic material, which is drawn up round the finger or instrument as it is passed downwards towards the aortic valve. The mortality by this procedure (14·7%) is appreciably lower than that by the transventricular route.

A method by which all three valves—aortic, mitral, and tricuspid—can be explored has been evolved and is described. A right-sided antero-lateral thoracotomy is performed, and through the right atrial appendage the tricuspid valve is explored and divided if stenosed. Through the same opening the aortic valve can be reached through an incision in the aorta. Lastly, the following ingenious method of approaching the mitral valve has been worked out: the sulcus between the atria is deepened by careful dissection and in the base of this an incision is made which is controlled by a purse-string suture, the finger being then passed into the left atrium and the mitral valve palpated and if necessary divided. At the same time the interatrial septum can be explored for unsuspected septal defect.

The selection of patients and the techniques of valvotomy are discussed in some detail. The authors' results suggest that more than 80% of the survivors show improvement over a follow-up period of one to 3 years. *T. Holmes Sellors*

1181. **A Correlative Study of Valvular Morphology and Clinical Results in Aortic Commissurotomy**
R. S. Litwak, J. F. Uricchio, and W. Likoff. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 781–786, April 26, 1956. 5 refs.

In a study carried out at Hahnemann Medical College and the Bailey Thoracic Clinic, Philadelphia, the authors have correlated some of the anatomical appearances noted at transaortic valvotomy with the late results in 40 patients (34 male and 6 female, aged 20 to 60 years) subjected to this operation. They found that the degree of calcification of the valve increased with advancing years, whereas limitation of mobility did not. Calcification was present to a greater or lesser extent in 35 (87%) of the patients and impairment of mobility in 28 (70%). Fusion of all three commissures was present in 30 (79%) of the patients, and in just under half (16 (42%) of 38 patients) the area of the aortic orifice was estimated as less than 0·5 sq. cm.

Valvotomy increased the opening in 24 cases (68·5%) to a size greater than 1·6 sq. cm., this figure being taken arbitrarily to represent an adequate anatomical result. Although generally the less the degree of calcification of the leaflets, the better is the chance of a satisfactory operation, nevertheless even in those with this complication an adequate split was achieved in 12 (52%) of those benefited.

Four of the patients died at operation and 7 died later, mostly of infective endocarditis. Of the 29 survivors, 23 were improved. As the authors point out, the dominant factor influencing the results was mobility of the valve, and so long as any mobility remained there was a possibility of improvement despite the presence of calcification. *J. R. Belcher*

1182. **Functional Evaluation of Mitral Valvulotomy. Superiority of the Treadmill Exercise Tolerance Test to Clinical and Resting Hemodynamic Evaluations in Selecting Patients**
R. A. Bruce, K. A. Merendino, J. J. Pampush, G. G. Bergy, and L. L. Brock. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 745–755, May, 1956. 4 figs., 15 refs.

The purpose of this report from the University of Washington, Seattle, is to show that physiological measurements of the functional effects of exercise under a standard work load are of more help than any other clinical or laboratory observations in deciding for or against surgical treatment of patients with symptoms due predominantly to mitral stenosis. A total of 52 patients who had undergone mitral valvotomy were followed up for periods of one month to 3 years, and at the end of the study classified according to the clinical course as improved, unchanged, worse, or died. Cardiac catheterization was carried out before operation in 27 cases, and it was found that except for a slightly higher cardiac index in the improved group, there were no differences between the 4 groups in resting haemodynamics. A treadmill ergometer was used for the exercise test. Patients who improved had had a very low endurance before operation; those who subsequently died exhibited a more marked reduction in endurance, together with subnormal respiratory efficiency during both rest and exercise. In contrast, exercise tolerance, measured before operation, was on the average more nearly normal in patients who were either unchanged or worse after surgery.

The calculation and use of the physical fitness index are described, and the values correlated with operative mortality and postoperative results. *R. G. Rushworth*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1183. **Disturbances of Cerebral Circulation in the Acute Stage of Myocardial Infarction.** (Расстройство мозгового кровообращения в остром периоде инфаркта миокарда)
M. Y. Melikova. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 23–30, No. 4, April, 1956. 6 figs.

A study of the clinical histories of 130 cases of cardiac infarction seen at the First Lenin Medical Institute, Moscow, showed that neurological disturbances were recorded in 31·4% of cases.

In a series of 14 personally studied cases of cardiac infarction with symptoms and signs suggestive of cerebral involvement the author found foci of cerebral softening in 5 cases and cerebral haemorrhages in 3; in the remainder the interference with cerebral circulation had a "dynamic" character [? transitory]. Of these 14 cases, 13 were fatal, and a histological study was carried out on the brain of 9 of these patients who, in the acute stage of cardiac infarction, showed no clinical features of cerebral involvement. The changes observed were tortuosity of small vessels (capillaries, arterioles, and small arteries), with localized dilatations, areas of stasis, oedema and focal homogenization of the vessel walls, perivascular oedema, diapedesis, and frank haemorrhages. These changes, which were moderate in the early hours of the attack, became more pronounced with time (36 to 72 hours). Cellular changes secondary to the vascular lesions were oedema of the nerve cells, oligodendroglial proliferation, and morphological changes in the astrocytes. All these changes apparently subside, since in cases examined post mortem 3 weeks after the attack haemosiderin deposits alone pointed to a previous circulatory lesion. *A. Swan*

1184. **The Prevention of Thromboembolic Complications in Myocardial Infarction by Anticoagulant Therapy. A Clinical-pathologic Study**
H. I. Glueck, H. W. Ryder, and P. Wasserman. *Circulation* [*Circulation (N.Y.)*] **13**, 884–895, June, 1956. 4 figs., 29 refs.

In an attempt to overcome the unreliability of the clinical diagnosis, and hence prognosis, of the complications following myocardial infarction, and to evaluate the effect of anticoagulant therapy in the prevention of such complications the authors, working at Cincinnati College of Medicine, Ohio, have analysed the necropsy records of 151 patients dying of myocardial infarction over an 8-year period. In 76 of these cases (the

" treated " group) anticoagulants had been given and in 75 (the " untreated " group) they had not, the two groups being similar in regard to age, sex, race, obesity, presence of heart failure, arrhythmia, previous attacks, and degree of shock.

Embolic complications which had been overlooked clinically were found frequently in these patients, but the use of anticoagulants had strikingly altered their incidence, from 41% in the untreated group to 9% in the treated group. The incidence of embolism judged by the pathologist to have been responsible for the death of the patient was reduced from 21% to 4%; likewise, the incidence of thrombophlebitis and mural thrombi was reduced by adequate anticoagulant therapy. In contrast, however, neither extension of the infarction (or the formation of a new infarct) nor the frequency of ventricular rupture appeared to be affected by this form of therapy.

The authors make a careful attempt to avoid drawing incorrect inferences from this type of case sample. Since the primary causes of death in the " treated " and " untreated " groups were the same (except for the sharp contrast of thrombo-embolic complications), they suggest that adequate anticoagulant therapy should be instituted early in cases of suspected infarction. As it was impossible to classify the patients clinically in regard to their eventual prognosis, they conclude that the main indication for the use of anticoagulants " is a clinical condition in which thrombo-embolism is a real hazard ".

P. Hugh-Jones

1185. **A Post-myocardial-infarction Syndrome. Preliminary Report of a Complication Resembling Idiopathic, Recurrent, Benign Pericarditis**

W. DRESSLER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1379–1383, April 21, 1956. 2 figs., 19 refs.

The author describes an unusual syndrome resembling benign pericarditis or the " post-commissurotomy syndrome " which was observed in 10 patients admitted to Maimonides Hospital, Brooklyn, New York, following a myocardial infarction. In 8 of the 10 cases a pericardial friction rub developed between the 3rd and the 24th days of the illness, persisted for a week or more, and in some cases recurred over a period of weeks. In 7 of the patients there was radiological evidence of pleural effusion, which was aspirated in 3 cases. Fever was prolonged after the initial infarction in 6 cases, in 2 a second rise of temperature occurred on the 9th and 15th days respectively, while in one case 8 weeks elapsed between the infarction and the onset of renewed fever. Pain, commonly of a pleuro-pericardial nature, was with fever the most consistent symptom and was felt at various sites, including the chest, jaw, arms, shoulders, and upper abdomen. A leucocytosis of as much as 35,000 cells per c.mm. occurred in 7 cases. The syndrome ran a prolonged course and showed a marked tendency to recur. From 2 to 6 febrile episodes were noted in some of the cases, and " flare-ups " of fever and pain were liable to occur over periods up to 9 months. Cortisone was found to terminate the fever and pain and to shorten the course of the syndrome. Three of the author's cases are described in detail and 3 similar cases reported in the literature are discussed. A warning is given that anticoagulant therapy, which may be resumed under the mistaken impression that the symptoms are due to extension of the infarction, is dangerous and is therefore contraindicated.

C. Bruce Perry

HEART FAILURE

1186. **Use of Intravenously Given Ganglionic Blocking Agents for Acute Pulmonary Edema. Preliminary Report**

M. H. ELLESTAD and W. H. OLSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 49–53, May 5, 1956. 2 figs., 6 refs.

Ganglion-blocking agents have been shown to reduce the increased venous return to the heart in such conditions as acute congestive failure and pulmonary oedema, but their use was condemned by Hilden (*Acta med. Scand.*, 1953, **147**, 175). The present authors, however, believe they still have a place in therapeutics.

At the Seaside Memorial Hospital (University of California School of Medicine), Los Angeles, 19 patients with pulmonary oedema were treated on 22 occasions by the intravenous injection of 2·5 mg. of hexamethonium chloride or 150 to 300 mg. of tetraethylammonium chloride. Recordings of the blood pressure and pulse and respiratory rates were made beforehand and every few minutes after the injection. In 12 cases the patient lost all symptoms of congestive failure and oedema within 30 minutes, and 7 were more comfortable but retained a few basal rales. Four patients died later, but death was not considered to have been accelerated by the treatment. In all cases there was a fall in blood pressure of about 50 mm. Hg in some 30 minutes. In one patient with cardiac asthma, 30 mg. of trimethaphan camphorsulphonate was given intravenously with good results. In none of the cases did the treatment cause undesirable hypotension. Of the two main agents used, tetraethylammonium was the more rapid in action and had a shorter duration of effect.

V. J. Woolley

1187. **Aminometradine in Treatment of Congestive Heart Failure**

M. M. PLATTS and T. HANLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 1078–1080, May 12, 1956. 3 figs., 6 refs.

The effect of aminometradine (" mictine ") on the urinary flow and excretion of electrolytes in 20 patients with congestive cardiac failure is described in this paper from Sheffield University. The quantity of fluid and salt ingested daily and the volume and electrolyte content of the urine over periods of 24 hours were measured before, during, and after treatment, which continued for 2 to 11 days. Aminometradine acts like a mercurial diuretic in that it increases urinary excretion of sodium and chloride without causing any increase in the glomerular filtration rate, presumably as the result of diminished reabsorption of sodium and chloride by the renal tubules. The diuresis produced by 400 to 800 mg.

of aminometradine daily was rather less than that produced by 2 ml. of mersalyl. The results in 18 of the cases are given in a table. A good therapeutic effect was obtained in 8, a fairly good response in 5, and a poor response in 5. In 3 cases nausea and vomiting necessitated withdrawal of the drug. The authors consider that the drug may be of value in cases of chronic cardiac failure. *H. E. Holling*

1188. **Treatment of the Low-salt Syndrome in Congestive Failure by the Controlled Use of Mercurial Diuretics**
A. L. RUBIN and W. S. BRAVEMAN. *Circulation* [*Circulation (N.Y.)*] **13**, 655–663, May, 1956. 3 figs., 9 refs.

The low-salt syndrome in patients with refractory congestive heart failure may result either from fluid retention with dilution of electrolytes or from excessive salt loss brought about by frequent administration of mercurial diuretics. In this paper from Cornell University Medical College a study of 25 cases of refractory cardiac failure is described, the results of which suggest that electrolyte dilution is the major factor in the aetiology of the low-salt syndrome. Responsiveness to mercurial diuretics can be restored by administration of acetazolamide (" diamox ") and ammonium chloride, which produces a rise in the plasma chloride level.
James W. Brown

1189. **The Effects of Intravenous Apresoline (Hydralazine) on Cardiovascular and Renal Function in Patients with and without Congestive Heart Failure**
W. E. JUDSON, W. HOLLANDER, and R. W. WILKINS. *Circulation* [*Circulation (N.Y.)*] **13**, 664–674, May, 1956. 3 figs., 8 refs.

The effect of intravenous administration of hydrallazine on cardiovascular and renal function and electrolyte and water excretion was studied at the Massachusetts Memorial Hospitals, Boston. In patients both with and without congestive heart failure the drug acted as a powerful renal vasodilator. The increased renal plasma flow was not necessarily dependent upon changes in cardiac output and arterial pressure, and usually there was no decrease in the excretion of sodium and water. The most satisfactory results with hydrallazine were obtained in hypertensive patients in congestive heart failure. *James W. Brown*

1190. **The Effect on the Renal Circulation of the Treatment of Heart Failure.** (Les consequences circulatoires rénales du traitement de l'insuffisance cardiaque)
J. LENÈGRE and J. HIMBERT. *Presse médicale* [*Presse méd.*] **64**, 625–627, April 4, 1956. 2 figs., 11 refs.

The authors report from the Hôpital Boucicaut, Paris, that investigation of renal function in 19 cases of heart failure treated either medically (9 cases) or surgically (10 cases) showed that an improvement in the cardiac condition was often accompanied by an increase of the previously depressed renal plasma flow. This increase was small in patients subjected to mitral commissurotomy (4 cases), but more striking after pericardiectomy (6 cases). The glomerular filtration fraction fell in some cases with reduction of the venous pressure. These haemodynamic improvements paralleled the increase in cardiac output in the 5 cases in which this was measured, but the renal haemodynamic pattern was seldom restored to normal. It is pointed out that the diuresis of successful therapy is not always correlated with a significant improvement in renal haemodynamics, and suggested that this fact seems to indicate that modification of renal tubular function may play a considerable part in the production of cardiac oedema.
J. McMichael

PERIPHERAL ARTERIES

1191. **The Treatment of Peripheral Arteriosclerosis. The Effect of Theobromine Magnesium Oleate on the Oscillogram of the Extremities.** (Zur Behandlung der peripheren Arteriosklerose. Über den Einfluss der Theobromin-Magnesiumoleat-Medikation auf das Oszillogramm der Extremitäten)
H. JANTSCH. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 776 and 785–786, May 18, 1956. 3 figs., 6 refs.

In a study of the effects of theobromine magnesium oleate on peripheral blood flow, carried out at the First University Surgical Clinic, Vienna, oscillometric measurments showed an increase in blood flow in 45 out of 64 patients treated for arteriosclerotic peripheral vascular disease. The drug was administered three times a day by mouth in doses of 0·2 to 0·4 g. As is the case with other vasodilators, it failed to save any limb in which the circulation was gravely impaired. *G. S. Crockett*

1192. **Neuropathy in Peripheral Vascular Disease. Its Bearing on Diabetic Neuropathy**
E. C. HUTCHINSON and L. A. LIVERSEDGE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 267–274, April, 1956. 6 figs., 10 refs.

On the relationship between peripheral vascular disease and diabetic neuropathy and other neurological changes widely divergent views have been expressed. At Manchester Royal Infirmary the authors have therefore investigated the neurological abnormalities in 90 patients with known peripheral vascular disease—all of them had intermittent claudication—those with frank gangrene, diabetes mellitus, or other cause of neurological disorder being excluded.

Of these 90 patients, 53 (58·8%) showed evidence of neurological abnormality in the lower limbs which was considered to be due to their vascular disease. However, the symptoms attributable to the neurological lesions were greatly overshadowed by those due to the vascular disease and in many cases had to be elicited by direct questioning. The neurological signs and symptoms tended to be more prominent on the side on which the vascular disease was most marked, and in some cases were present only when the claudication had been produced by exercise. In 11 cases there was subjective sensory disturbance only, without abnormal signs, while abnormal signs such as absent or diminished reflexes or alteration of sensation in the legs were present in 42.

No definite correlation could be established between age and neurological abnormalities in this series, the patients' ages ranging from 40 to 80 years.

The authors stress the mild nature of the neurological disease despite the advanced state of the peripheral vascular disease, and point out that a proportion of the neurological signs and symptoms in diabetic patients may be due to peripheral vascular disease rather than to diabetic neuropathy. *G. S. Crockett*

1193. **A Critique on the Therapeutic Value of Lumbar Sympathectomy**
A. R. NELSON and I. R. TRIMBLE. *Surgery* [*Surgery*] **39**, 797–804, May, 1956. 16 refs.

With reference to the treatment of peripheral vascular disease the authors present an analysis of the results of lumbar sympathectomy performed during the years 1946 to 1951 at the Johns Hopkins Hospital, Baltimore, in 192 (out of 251) patients for whom adequate follow-up results for 2 years or more were available. These results are tabulated in terms of the leading symptoms in treated limbs. There were 63 patients with arteriosclerosis, 53 with arteriosclerosis complicated by diabetes, 7 with thromboangiitis obliterans, 42 with postphlebitic syndrome, 8 with causalgia or trauma, and a miscellaneous group of 18. A result was considered satisfactory if the symptom concerned showed any improvement and did not relapse in the course of 2 years.

The proportions of patients in each group considered to have been benefited by the operation, which usually involved removal of the 2nd to 4th lumbar ganglia, were as follows: arteriosclerosis 37%, arteriosclerosis complicated by diabetes 22%, Buerger's disease 29%, and postphlebitic syndrome 24%; the 3 patients with causalgia were all completely relieved, but the result was good in only 2 of the 5 traumatic cases. Of patients with arteriosclerosis the final results were considered to be doubtful or poor in 63%, of those with diabetes in 74%, they were poor in 5 cases of Buerger's disease (71%), and in 76% of the postphlebitic group. In view of these findings the authors come to the conclusion that they cannot support the operation of lumbar sympathectomy "with much enthusiasm". Moreover, they state that from the results in this series no means of forecasting the result of the operation in any particular individual could be established. *C. J. Longland*

HYPERTENSION

1194. **Divided Renal Function Studies in Hypertension**
I. G. GRABER and R. SHACKMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 1321–1326, June 9, 1956. 9 figs., 17 refs.

The authors, at the Postgraduate Medical School of London, made a special study of 13 hypertensive patients who, because of suspected unilateral renal disease, were referred for consideration of nephrectomy. In addition to the usual clinical and laboratory tests of renal function, cystoscopy and ureteric catheterization were carried out, and separate measurements were made of the clearance by each kidney of inulin, *para*-aminohippurate, and endogenous creatinine. Of the 13 patients, 5 were subjected to unilateral nephrectomy, and 3 of these, who were followed up for 14 months to 2 years, appeared to benefit from the operation. In the remaining 8 patients operation was proscribed because there was functional impairment of both kidneys. In 11 out of 13 single kidneys considered to be normal by excretion urography significant functional abnormalities were found by divided clearance studies. This finding was usually the decisive factor in advising against removal of the other kidney. Stressing this point—namely, that normal excretory urograms are often obtained where there are significant functional changes—the authors find it difficult to avoid the conclusion that divided renal function studies should be carried out before nephrectomy is advised as a treatment for hypertensive disease. As they point out, however, the procedure requires great technical skill, full laboratory facilities, and fortitude on the part of the patient. *Bernard Isaacs*

1195. **The Effect of Prolonged Adherence to a Salt-free Diet on Life Expectancy in Essential Hypertension.** (Lebensaussichten von essentiellen Hypertonikern bei jahrelang eingehaltener salzfreier Diät)
H. SARRE, W. KAMPMANN, and G. SCHMIDT. *Klinische Wochenschrift* [*Klin. Wschr.*] **34**, 509–511, May 15, 1956. 3 figs., 28 refs.

In this paper from the University Medical Clinic, Freiburg-im-Breisgau, are reported the results of a 9-year follow-up study of 45 patients with essential hypertension who had been treated for a number of years with Volhard's salt-free diet under supervision of the staff of Volhard's own clinic. Proof of adherence to the diet was obtained by estimation of the urinary chloride excretion during the first few days after readmission to hospital; in 14 cases this was less than 1 g. in 24 hours, under 1·4 g. in 16 cases, under 2 g. in 10 cases, and less than 3 g. in the remaining 5. A group consisting of 45 patients who had failed to adhere to the diet served as a control, the two groups being comparable in respect of the severity of the hypertension and of its complications; 30 patients in each group had a diastolic pressure of over 120 mm. Hg when first seen, while 15 patients in the control group and 16 in the treatment group had some degree of cardiac failure. The groups were less closely matched in respect of the number with cardiac infarcts, cerebrovascular accidents, and renal impairment, but eye-ground changes were evenly distributed, 12 patients from the control group and 11 from the treatment group having a Grade-III or -IV retinopathy. [Unfortunately no mention is made of the age and sex distribution.]

It was shown that the difference in the expectation of life between the two groups was statistically significant for the first 3 years of treatment, 20 patients from the control group, compared with 9 from the treatment group, having died during this period. As might be expected, these deaths occurred mostly among the more severe cases, all but 2 in each group being of patients with a diastolic pressure of over 120 mm. Hg (Phases IV

and V in the classification of Sarre and Lindner). In the succeeding years, however, the mortality in the treatment group exceeded that among the controls, so that at the end of the 9-year period the number of survivors from each group was almost identical, namely, 11 in the control group and 12 in the treatment group. Analysis of the cause of death showed a marked similarity between the groups, 17 patients in the control group dying in cardiac failure, 8 from cerebrovascular accidents, and 3 from renal failure; the corresponding figures for the treatment group were 17, 7, and 5 respectively.

The authors conclude that treatment with a salt-free diet does not alter the ultimate course of essential hypertension, but does tend to increase the expectation of life by some 2 to 3 years in the more severe cases.

H. F. Reichenfeld

1196. **The Effects of Chronic Pentapyrrolidinium-induced Hypotension on Renal Hemodynamics and on the Excretion of Water and Electrolytes in Hypertension**
J. W. Stover, R. W. Griffin, and R. V. Ford. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 893–898, May, 1956. 2 refs.

Renal function and excretion of water and electrolytes were studied at Baylor University College of Medicine, Houston, Texas, in 11 hypertensive patients receiving pentapyrrolidinium (pentolinium) tartrate, the glomerular filtration rate, renal plasma flow, maximal tubular excretory capacity, rate of urine formation, sodium and potassium excretion, and blood-pressure changes being observed before and after treatment. With the patient in the supine position there was no reduction in renal plasma flow, glomerular filtration rate, or tubular excretory capacity, although there was a significant fall in blood pressure. From this the authors conclude that the renal blood vessels of hypertensive patients are still able to respond to pentolinium tartrate by vasodilatation. After treatment there was a marked decrease in excretion of sodium with a moderate decrease in that of water, without any accompanying clinical change.

In the authors' view these changes can be accounted for by the low sodium intake of these patients. Further oral administration of pentolinium tartrate cannot be regarded as producing any significant changes in water or electrolyte excretion in hypertensive patients with normal renal function. *J. Warwick Buckler*

1197. **Reserpine in Severe Hypertension**
R. Platt and H. T. N. Sears. *Lancet* [*Lancet*] **1**, 401–403, April 14, 1956. 3 figs., 5 refs.

At the Royal Infirmary, Manchester, 41 patients with moderately severe hypertension received reserpine alone in a dose of 0·5 to 2 mg. daily; 13 other patients with malignant hypertension were given reserpine in addition to ganglion-blocking agents. Of the 41 patients in the first group, 17 responded well, the mean fall in diastolic blood pressure being 47·4 mm. Hg. Of the 13 patients in the second group, 9 responded favourably when reserpine was given in addition to a ganglion-blocking agent, and in 2 of these it was possible to discontinue the latter. Symptomatic improvement was observed in most of the patients, including some of those whose blood pressure did not fall. The authors state that there were no clinical criteria whereby it was possible to forecast which patients would respond favourably to reserpine. Treatment had to be stopped because of mental depression in 10 patients, one of whom committed suicide. Lactation was observed in 3 females.

It is concluded that reserpine has a significant hypotensive action in 40% of cases of severe hypertension; that in the most severe cases it should probably be given with other drugs; and that it should not be used in cases of mild hypertension. *Bernard Isaacs*

1198. **Mecamylamine, a New, Orally Effective, Hypotensive Agent. Experimental and Clinical Evaluation**
E. D. Freis and I. M. Wilson. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 551–561, May, 1956. 4 figs., 10 refs.

"Mecamylamine", a readily-absorbed ganglion-blocking agent, was tried in the treatment of hypertension at the Georgetown University and Veterans Administration Hospitals, Washington, D.C. In 9 hypertensive patients a single intravenous dose of 15 to 20 mg. of the drug caused a significant reduction in blood pressure in the supine position and a marked postural hypotension lasting 6 to 12 hours. A somewhat smaller dose by mouth had a similar effect, the reduction in blood pressure lasting 4 to 12 hours. In further experiments it was found that mecamylamine abolished or reduced the hypertensive "overshoot" following the Valsalva manœuvre, but had an inconstant influence on three other sympathetic vasoconstrictor responses—the cold pressor response, the skin temperature gradient between umbilicus and digits on exposure to cold, and the reduction in digital volume on inspiration.

Mecamylamine was given by mouth in an average daily dose of 29 mg. (range 3 to 90 mg.) for periods of 4 weeks to 4 months to 36 patients with moderately severe or severe hypertension. Satisfactory reduction in blood pressure was obtained in all cases, and in some instances improvement in the optic fundi, heart size, electrocardiogram, and renal function. Tolerance to the drug was absent or slight. The treatment of 4 patients had to be stopped because of side-effects. Almost all patients complained of constipation during treatment; other side-effects experienced by about a quarter of the patients included postural faintness, disturbances of accommodation, dry mouth, difficulty in micturition, and impotence.

Of 19 hypertensive patients given mecamylamine by mouth after receiving pentolinium tartrate by mouth for 6 months or longer, 14 preferred the former drug because of its more uniform hypotensive action. The authors state that although mecamylamine was more completely absorbed by mouth than were other ganglion-blocking agents, it was no less liable, in effective hypotensive doses, to cause troublesome side-effects.

[For measurements of the skin temperature gradient the temperature of the cold room is stated, presumably in error, to be 63° to 71° C.] *Bernard Isaacs*

Haematology

1199. **Some Effects of Severe Chronic Anaemia on the Circulatory System**
W. WHITAKER. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 175–183, April, 1956. 25 refs.

Changes in the general and renal circulations were investigated at the Royal and the City General Hospitals, Sheffield, in one male and 9 female patients with severe chronic anaemia, of whom 8 had pernicious anaemia, one carcinomatosis, and one chronic gastro-intestinal bleeding. In 4 cases there was evidence of congestive cardiac failure. Cardiac output was measured in 9 cases, employing the Fick principle, right auricular blood samples being obtained by cardiac catheterization. Renal blood flow was calculated from the effective renal plasma flow and the haematocrit reading.

The cardiac output was high in 7 out of the 9 cases and fell with treatment of the anaemia. The author considers that the high cardiac output is a mechanism whereby the total oxygen consumption is maintained at a normal level despite the fact that the anaemia reduces the oxygen-carrying capacity of the blood. As the heart rate was not greatly increased it is thought that the high cardiac output was maintained by an increased stroke volume. When the cardiac output fell with treatment there was little change in the right auricular pressure in 2 cases, indicating that the high output was independent of the elevation of venous pressure. Marked hypertension developed in some cases following treatment of the anaemia, suggesting that the latter had masked or predisposed to the condition. Renal blood flow was reduced in all cases, but improved with treatment of the anaemia. It is suggested that this renal anoxia may account for the hypertension, and for the retention of salt and water which gives rise to the signs of congestive cardiac failure in anaemic patients.
G. S. Crockett

1200. **The Treatment of Thrombocytopenic Haemorrhage by the Injection of Human Fibrinogen in High Dosage.** (Le traitement des hémorragies thrombocytopéniques par l'injection de fibrinogène humain à fortes doses)
P. CAZAL, R. GRAAFLAND, P. IZARN, M. MATHIEU, G. PALEIRAC, and J. FISCHER. *Presse médicale* [*Presse méd.*] **64**, 670–671, April 11, 1956. 2 figs., 5 refs.

The authors describe the treatment of certain haemorrhagic conditions associated with thrombocytopenia with a preparation of fibrinogen in the form of Cohn's Fraction I; this non-purified fraction contained 60% of fibrinogen together with a little active plasmin and the antihaemophilic factor. To 4 patients during 10 episodes of thrombocytopenic bleeding intravenous injections of this fibrinogen preparation were given in doses of 3 to 10 g.; haemostasis was produced on 9 occasions. Although the mechanism of this action of fibrinogen is not known, the authors suggest that in vascular thromboses the reduction in the number of platelets may be compensated for by an excess of fibrinogen. They point out, however, that in all 4 cases the patient's blood fibrinogen value was normal. Details of 3 illustrative case histories are given. *John F. Wilkinson*

1201. **Revival of Stored Blood with Guanosine and Its Successful Transfusion**
T. A. J. PRANKERD. *Lancet* [*Lancet*] **1**, 469–471, April 21, 1956. 4 figs., 8 refs.

It has already been shown that in blood incubated for 24 hours erythrocyte metabolism ceases, but that it continues in the presence of the nucleosides, adenosine and guanosine, the nucleosides providing ribose phosphate which is utilized by the erythrocytes for glycolysis. In this paper from University College Hospital Medical School, London, further observations on the revival of stored blood are reported. At various times after 3 weeks' storage 5 μmols of adenosine or guanosine in isotonic saline solution was added for each millilitre of stored blood and the mixture incubated for one hour. To estimate post-transfusion survival 30 μc. of radioactive sodium chromate ($Na_2{}^{51}CrO_4$) was added to 10 ml. of revived blood and allowed to stand for one hour. The washed cells were suspended in saline and injected into a healthy recipient. Samples of blood were taken from the recipient at intervals for 2 days and the radioactivity was estimated. The increased survival of the nucleoside-treated cells at the end of 48 hours, compared with cells incubated with glucose only, was obvious.

Adenosine was more toxic than guanosine, the latter being non-toxic to man. In cats there was a fall in blood pressure after intravenous administration of adenosine, but not after guanosine. *Kate Maunsell*

1202. **Preservation of Red Cells at −79°C.**
H. CHAPLIN, H. CRAWFORD, M. CUTBUSH, and P. L. MOLLISON. *Clinical Science* [*Clin. Sci.*] **15**, 27–39, 1956. 1 fig., 17 refs.

1203. **Anti-A Agglutinins in Pooled Plasma as a Cause of Hemolytic Anemia**
J. RUTZKY, F. COHEN, and W. W. ZUELZER. *Blood* [*Blood*] **11**, 403–422, May, 1956. 14 figs., 31 refs.

The administration of pooled plasma to persons of all ABO blood groups has been regarded as safe because the anti-A and anti-B isoantibodies have been assumed to be diluted and probably neutralized. At the Children's Hospital of Michigan, Detroit, however, the authors have observed the development of haemolytic anaemia in Group-A recipients after prolonged administration of large amounts of pooled plasma, which was found to have an anti-A titre of 1 in 64 or higher. They therefore conclude that the prolonged administration of pooled plasma to recipients of Group A is dangerous, and

further suggest that there may be a similar, but less common, risk to recipients with blood of Group B.

A. Piney

NEOPLASTIC DISEASES

1204. **Prognosis of the Malignant Lymphomas**
C. A. HALL and K. B. OLSON. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 687–706, April, 1956. 2 figs., 27 refs.

The authors discuss the factors to be considered when attempting to assess the prognosis of patients suffering from malignant lymphoma. At the Veterans Administration Hospital, Albany, New York, they have studied 116 cases of this type of tumour and correlate their findings with those reported by other workers. Both pathological and clinical features must be taken into account, but even with full knowledge of these an exact prediction cannot be made. For example, the histological appearances, especially in Hodgkin's disease, may change during the course of the illness and may differ at different sites in the body at any one time. Differences of terminology add further difficulties in comparing groups of cases, which are increased by such personal factors as the interest and experience of the histologist. A clinical and pathological picture of Hodgkin's paragranuloma or of giant follicle lymphoma alone warrants some optimism in prognosis. The extent of the disease and the response to initial treatment, together with the severity of constitutional symptoms, are of some prognostic help. In Hodgkin's disease the prognosis is rather poorer in older patients. Unassessable factors, such as the resistance of the patient to his disease, may alter the outlook in any given case.

[This is a useful discussion. The original paper should be consulted for detailed tables of survival times.]

R. B. Thompson

1205. **Treatment of Chronic Granulocytic Leukemia with 1:4-Dimethanesulfonyloxybutane (Myleran)**
R. F. SCHILLING and O. O. MEYER. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 986–989, May 24, 1956. 7 refs.

The authors report from the University of Wisconsin, Madison, that during the past 4½ years they have treated 19 cases of chronic granulocytic leukaemia with "myleran". In most of the cases 4 to 6 mg. was given orally daily until the haemoglobin level had risen to near normal. No attempt was made to reduce the leucocyte count to normal, although this was sometimes achieved before a normal haemoglobin level was reached. Therapy was temporarily discontinued if the leucocyte count fell below 10,000 per c.mm. It is now the authors' usual practice to continue maintenance therapy with doses of 1 to 4 mg. daily. In 9 of these cases no previous treatment had been given.

Excellent remissions lasting from 4 to over 30 months, with subjective improvement, rise in the haemoglobin level, gain in weight, decrease in the size of the spleen, and a fall in the leucocyte count occurred in 10 of the patients; of these, 7 are still alive, one has died of leukaemia, one from bronchogenic carcinoma, and one of glioblastoma multiforme after 9 months of therapy. Fair to good remissions occurred in 4 cases. In the remaining 5 cases treatment with myleran was considered a failure; 2 of these patients had thrombocytopenia, one myelofibrosis, one died of cerebral haemorrhage, while in the fifth case the diagnosis was equivocal. Purpura and other toxic manifestations were not observed, except possibly in one case in which the bone-marrow showed hypoplasia, and the administration of the compound caused no discomfort to the patients. It was noted that recent cases appeared to respond best to the treatment.

A. Ackroyd

1206. **On the Use of Radioactive Phosphorus in Chronic Leukaemias.** (К вопросу о применении радиоактивного фосфора при хронических лейкозах
V. K. KARNAUKHOV. *Советская Медицина* [*Sovetsk. Med.*] 42–45, No. 4, April, 1956.

At the M. F. Vladimirskij Regional Clinical Institute, Moscow, 28 selected patients suffering from chronic leukaemia were treated with radioactive phosphorus (^{32}P) and remained under observation for from one to 2½ years; 7 of the patients had previously been treated by other methods, such as urethane and *x*-irradiation. The ^{32}P was given orally in the form of a watery solution of disodium hydrogen phosphate in a dose of 1·5 millicurie weekly for 4 to 6 weeks, the average total dose being 6 millicuries.

Of the 19 patients with chronic myeloid leukaemia, 16 showed varying degrees of clinical and/or haematological improvement, the remission lasting from 3 to 14 months; no improvement occurred in the remaining 3 patients. There were no complications. A second course of treatment with ^{32}P was given to 2 of the patients 4 and 4½ months respectively after the first, but the effect of this was less pronounced and the remission obtained was shorter than on the first occasion. Ten of the patients were subsequently treated with *x*-ray therapy, but 4 died in from 4 to 24 months after treatment with ^{32}P from an acute exacerbation of the disease. Of the 9 patients with chronic lymphatic leukaemia, clinical remission was obtained in 6 which lasted from 3 to 10 months. Again the effects of a second course of treatment given later in 2 cases were less beneficial. Of the 3 patients in whom there was no improvement following treatment, one died within a month as a result of progression of the leukaemia and the other 2 developed severe hypoplastic anaemia, one of these subsequently dying from this disease in spite of energetic therapy.

The author concludes that the administration of radioactive phosphorus provides a simple and effective method of treatment which gives results comparable to those of radiotherapy and which is particularly suitable for chronic myeloid leukaemia. It is not suitable, however, for the treatment of acute or subacute leukaemias or of acute exacerbations of the chronic forms, and it should be used with caution in the treatment of chronic lymphatic leukaemia in view of the danger of aplasia of the bone marrow.

Marcel Malden

ANAEMIA

1207. **Erythrokinetics: Quantitative Measurements of Red Cell Production and Destruction in Normal Subjects and Patients with Anemia**
E. R. GIBLETT, D. H. COLEMAN, G. PIRZIO-BIROLI, D. M. DONOHUE, A. G. MOTULSKY, and C. A. FINCH. *Blood* [*Blood*] **11**, 291–309, April, 1956. 2 figs., 35 refs.

The authors, writing from the University of Washington, Seattle, have devised the term " erythrokinetics " to describe " the over-all activity of cell production and destruction within the erythron ". In an attempt to define quantitatively the erythrokinetics of normal man and of patients with anaemia the erythrocyte turnover of 19 normal subjects and 25 anaemic patients was studied, the erythroid : myeloid ratio of the bone marrow, reticulocyte count, plasma iron turnover, utilization by erythrocytes of radioactive iron (^{59}Fe), and excretion of urobilinogen being estimated.

They conclude that erythropoiesis must be defined in terms of the total quantity of erythrocytes produced (total erythropoiesis) and of the portion of erythrocytes produced in the marrow which is delivered to the circulating blood (effective erythropoiesis). The normal marrow appears to be able to increase its effective production of erythrocytes to 3 times the normal in acute anaemia and 6 times the normal in chronic anaemia, but in many disease states this response is impaired. Where a quantitative defect alone exists a normal ratio is maintained between effective and total erythropoiesis, all the erythrokinetic indices undergoing changes of similar magnitude. Dyshaematopoiesis of the marrow on the other hand is characterized by dissociation of the erythrokinetic indices, those values which reflect total erythropoiesis, such as plasma iron turnover, urobilinogen excretion, and erythroid : myeloid ratio of the marrow, being considerably greater than those which represent effective erythropoiesis, such as the reticulocyte count and erythrocyte utilization of radioactive iron.

[This paper is long and complex; it requires detailed study.] *Janet Vaughan*

1208. **Atypical Familial Hemolytic Anemia**
R. K. SMILEY, H. DEMPSEY, P. VILLENEUVE, and J. S. CAMPBELL. *Blood* [*Blood*] **11**, 324–337, April, 1956. 3 figs., 23 refs.

The authors describe the genetic, clinical, and haematological features of an atypical form of familial haemolytic anaemia occurring in 2 siblings studied at Ottawa General Hospital. Both were seen in the first year of life with severe anaemia and enlargement of the spleen, which in one child reached the iliac fossa. Other members of the family were found to have splenomegaly, but without anaemia, icterus, or reticulocytosis. The anaemia was normocytic, normochromic, and not associated with any characteristic abnormality of the erythrocytes. There was only a very slight increase in osmotic and incubated mechanical fragility of the erythrocytes, which was lost after splenectomy. The survival time of the patients' own erythrocytes was not examined, but in one case the survival of normal cells in the patient's circulation was decreased before and became normal after splenectomy. As in some rather similar reported cases the patients had French-Canadian ancestry and Group-A blood.

The authors suggest that the anaemia was due to an intrinsic abnormality of the erythrocytes, resulting in a decreased life span, together with some extracorpuscular factor, possibly located in the spleen. They postulate some form of dominant inheritance, but emphasize the features of low penetrance and expressivity of the trait.
Janet Vaughan

1209. **Gastric Lesion in Some Megaloblastic Anemias. Results of Follow-up Examinations.** [In English]
M. SIURALA. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 337–348, June 9, 1956. 5 figs., 7 refs.

The author has previously shown that atrophic changes in the gastric mucosa and histamine-fast achlorhydria frequently occur in patients with pernicious anaemia due to infestation with tapeworms. In order to determine the relationship of these changes to the presence of tapeworms 26 patients, 9 male and 17 female, ranging in age from 19 to 76 years seen at the 2nd Medical Clinic, University of Helsinki, with this type of anaemia were studied before and after expulsion of the worm, haematological and neurological examinations, gastric biopsy, and an augmented histamine test meal being carried out. Gastroscopy was also performed on all patients at the first examination and on 10 at the second examination.

In 21 of the cases the haematological and neurological findings were essentially normal at the second examination, the interval between the two examinations averaging 9 months. Of 19 of these adequately treated patients the mucosal atrophy had diminished in 8, was unchanged in 8, and had progressed in 3, while of 4 patients considered to have been inadequately treated none showed improvement, 3 being unchanged and one being worse. Inflammatory signs improved in 11 out of 18 adequately treated cases and remained unchanged in 7; of 5 inadequately treated cases the inflammatory signs remained unchanged in 3 and increased in 2. These findings were supported by the results of gastroscopic examination in the 10 cases in which it was carried out. There was some correlation between the degree of inflammation and the degree of mucosal atrophy, but there were many individual exceptions. The author agrees that the results do not exclude the possibility that the inflammation and the mucosal atrophy may be parallel responses to the same causative condition. However, the disappearance of inflammatory signs after expulsion of the tapeworm supports the view that, in many cases, the tapeworm is the cause of the inflammation.

The histamine test meal showed that free hydrochloric acid was present at both examinations in 2 out of the 26 cases and at the second examination only in 9 cases, free acid returning in 5 of the patients showing mucosal improvement and in 4 showing no improvement. These results suggest that the histamine-fast achlorhydria common in these patients may be due to an inhibition resulting from the presence of the tapeworm or to an associated deficiency state rather than to mucosal destruction.

Similar investigations on one patient with intestinal megaloblastic anaemia before and after successful treatment with aureomycin showed a reversion to normal of a previous marked gastric atrophy with superficial inflammation. Another patient with megaloblastic anaemia following partial gastrectomy, who was successfully treated with cyanocobalamin and iron, showed no improvement in the gastric mucosa, and the histamine-fast achlorhydria persisted. For comparison, 10 previously untreated cases of Addisonian pernicious anaemia were examined after successful treatment with cyanocobalamin for 2 to 14 months. In 7 cases no normal gastric glands were present before or after treatment, in 2 cases the mucosal atrophy had progressed, while in the seventh case there was no change in the mucosal condition. These findings agree with those of other investigators.

M. Lubran

1210. **Intestinal Absorption and Hepatic Uptake of Radioactive Vitamin B_{12} in Various Age Groups and the Effect of Intrinsic Factor Preparations**

C. B. J. GLASS, A. A. GOLDBLOOM, L. J. BOYD, R. LAUGHTON, S. ROSEN, and M. RICH. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 124–133, March–April, 1956. 3 figs., 17 refs.

The hepatic uptake after oral administration of vitamin B_{12} (cyanocobalamin) labelled with radioactive cobalt (^{60}Co) has been studied in 60 subjects between the ages of 18 and 90; these were either healthy or suffering from diseases irrelevant to the study. There was no marked impairment of absorption of cyanocobalamin in the older age groups, but a tendency for some reduction after the age of 60 was noted. Of 30 subjects aged over 60 in whom gastric acidity was determined, this reduction in the absorption of cyanocobalamin was greater in the 16 showing hypoacidity or anacidity than in the 14 with normal acidity. Administration of an intrinsic-factor preparation with the cyanocobalamin resulted in a 25% increase in hepatic uptake of the vitamin in 20 of 44 subjects drawn from all age groups; in 20 others no significant change occurred, and a decrease in absorption was found in 4 subjects. When the intrinsic-factor preparation was given to 17 subjects, mostly over the age of 60, who had gastric hypoacidity or anacidity, there was a strikingly significant increase in absorption. *F. W. Chattaway*

1211. **The Urinary Excretion Test for Absorption of Vitamin B_{12}. I. Reproducibility of Results and Agewise Variation. II. Effect of Crude and Purified Intrinsic-Factor Preparation**

B. F. CHOW, J. P. GILBERT, K. OKUDA, C. ROSENBLUM, W. L. WILLIAMS, and R. GRASBECK. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 142–150, March–April, 1956. 22 refs.

In the first of these papers on the urinary excretion test for absorption of vitamin B_{12} (cyanacobalamin), the reproducibility of results and variation of absorption with age are discussed. The urinary excretion of orally administered radioactive vitamin B_{12} was determined by the method of Schilling in a group of young males aged 17 to 30 years with comparable dietary histories and in a group of aged males. In repeated tests on the same individuals there was good reproducibility of results. No significant variation in absorption with age was noted, although in a few of the subjects in the older group there was very low absorption. Simultaneous administration of intrinsic-factor preparations did not reveal any marked changes in absorption of the radioactive vitamin, a small increase being noted in some subjects and a small decrease in others.

In the second paper an investigation of the effect of intrinsic factor on vitamin B_{12} absorption is reported. The urinary excretion of radioactive vitamin B_{12} in 91 healthy male volunteers was estimated by the Schilling technique after oral administration of the vitamin with or without intrinsic-factor preparations. With doses of 50 μg. of vitamin B_{12} and certain crude preparations of intrinsic factor there was a significant decrease in absorption of the vitamin. When, however, a highly purified preparation of intrinsic factor was used a significant increase in excretion was observed. The purified preparation was still capable of binding vitamin B_{12}.

F. W. Chattaway

1212. **The Urinary Excretion Test in the Diagnosis of Addisonian Pernicious Anemia**

S. F. RABINER, H. C. LICHTMAN, J. MESSITE, R. J. WATSON, V. GINSBERG, L. ELLENBOGEN, and W. L. WILLIAMS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 437–445, March, 1956. 2 figs., 13 refs.

The authors of this paper describe a test for the diagnosis of pernicious anaemia in haematological remission which is based on the inability of the patient with this disease to absorb orally administered cyanocobalamin (vitamin B_{12}). A dose of 2 μg. of vitamin B_{12} labelled with radioactive cobalt is given by mouth, followed by an intramuscular injection of 1,000 μg. of non-radioactive vitamin B_{12} (" flushing dose ") on two successive days. It was found that a mean of 13·3% of the dose of radioactive vitamin was excreted in the urine of healthy subjects, whereas the figure for patients with pernicious anaemia was 0·85%. Further, when a potent intrinsic-factor preparation was added to the radioactive vitamin B_{12}, patients with pernicious anaemia excreted an average of 8·2% of the dose of the vitamin.

In this test urine was collected over a total period of 4 days, including a preliminary control day. No overlap was noted between the results from healthy subjects and those obtained in cases of pernicious anaemia, thus permitting a definite diagnosis. The test has been found useful in disproving a diagnosis of pernicious anaemia which had been reached on insufficient grounds. In patients with megaloblastic anaemia not due to absence of intrinsic factor the test showed normal urinary excretion. *John Naish*

1213. **Hemoglobin in Pernicious and Allied Anemias. The Significance of an Abnormal Alkali Denaturation Curve**

O. H. IVERSEN and G. LARSEN. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **8**, 159–167, 1956. 6 figs., 27 refs.

Respiratory System

1214. **Enzyme Therapy by Intramuscular Route in Chest Diseases**
N. E. SILBERT. *Diseases of the Chest* [*Dis. Chest*] **29**, 520–532, May, 1956. 7 refs.

Trypsin was given by intramuscular injection to 25 patients, including one child, with chronic bronchial asthma in an attempt to determine whether this would bring about liquefaction of thickened bronchial mucus. A preparation containing 5 mg. of trypsin per ml. of sesame oil was injected into the buttocks as follows: a first injection of 0·5 ml. was given, and in the absence of side-effects 1 ml. was injected daily for 5 to 7 days, followed by 1 ml. on alternate days for 2 weeks and a final injection one week later. Children received half this dosage for a shorter period. Two courses of treatment were required in 7 cases and three courses in 5. There were no gross side-effects apart from pain at the injection site, maculopapular rashes, and dizziness. Marked clinical and radiological improvement was obtained in 13 patients and slight improvement in 9; in 3 the condition was unchanged. There was no improvement in the emphysema. The consistency of the sputum improved and the volume lessened after a few days' treatment.

[There is no real evidence of the value of trypsin in asthma. Chronic asthmatics are, of course, very suggestible to any new form of treatment.] *I. M. Librach*

1215. **Effect of Oxygen on Exercise Ability in Chronic Respiratory Insufficiency. Use of Portable Apparatus**
J. E. COTES and J. C. GILSON. *Lancet* [*Lancet*] **1**, 872–876, June 9, 1956. 7 figs., 12 refs.

When patients with severe respiratory insufficiency breathe oxygen their arterial oxygen saturation is restored to normal, the uptake of oxygen during exercise is increased, the ventilation required for a standard exercise is reduced, and sometimes the ability to carry out exercise is greatly improved. In the study described in this paper from Llandough Hospital, Penarth, Glamorganshire, the authors have sought to evaluate the usefulness of portable oxygen-breathing equipment to such patients. The two types of apparatus used, which weighed from 2½ to 3½ lb. (1·1 to 1·6 kg.), are described and illustrated.

In 22 out of 29 severely disabled men with pneumoconiosis or bronchitis and emphysema exercise ability was much increased by breathing oxygen. Thus men virtually incapacitated by breathlessness were able to move about the house and to walk out to the garden. The reduction in pulmonary ventilation produced by breathing oxygen causes a rise in arterial carbon dioxide tension, and this could lead to loss of consciousness. This danger was obviated in the present study by using 30% oxygen and restricting its use to essential tasks, and no untoward incidents occurred. In studies of the minimal effective oxygen flow and of the influence of the design of the oxygen mask it was shown that the effect of 30% oxygen was not greatly inferior to that of 50% or 100% oxygen in increasing exercise ability; this can be obtained from an oxygen flow of 4 litres per minute delivered to a well-fitting oxygen mask with an oxygen reservoir bag protected by a check valve to prevent rebreathing. Such portable oxygen equipment has been used successfully by 4 of the patients in their own homes, and no adverse effects have so far been observed. The trial is continuing.

T. Semple

INFLAMMATORY DISEASES

1216. **Pulmonary Brucellosis**
A. E. GREER. *Diseases of the Chest* [*Dis. Chest*] **29**, 508–519, May, 1956. 8 figs.

Clinical and other findings in 41 cases of pulmonary brucellosis, details of which were obtained from 13 doctors in response to a questionary sent to 700 chest specialists in the United States, were compared with those in 27 new cases not previously published, including 18 treated by the present author and 9 seen at the Veterans Administration Hospitals at Louisville, Kentucky, and Houston, Texas. The most prominent symptoms in all the cases were fever, chills, cough, chest pain, hoarseness, choking sensations, digestive disturbances, and arthritic pain. Of the 41 patients in the former series, 38 were farmers, ranchers, or meat-packers; the occupations of the remainder were not connected with cattle, sheep, or pigs. In 30 of the 41 cases fever was intermittent, while in 11 it was remittent. Infection was due to *Brucella abortus* in 36 cases, to *Br. melitensis* in 3, and to *Br. suis* in 2 [no evidence provided]. Blood culture was positive in only 8 cases, and in these the condition was acute. The author states that the intradermal test was performed in most cases [but no results are given]. The blood count showed a moderate anaemia and lymphocytosis, but the erythrocyte sedimentation rate was little changed. Chest radiographs revealed evidence of pneumonitis, pneumonia, localized granuloma (one case), bronchial obstruction by enlarged lymph nodes, pleural and perihilar thickening, and peribronchial infiltration. Treatment in the 11 acute cases consisted in administration of antibiotics (streptomycin and aureomycin) only, or a combination of this and surgery (decortication and resection). The average duration of treatment in 4 of the acute cases was 19 days. On the whole, treatment appeared to be moderately successful in the acute cases, but was satisfactory in only half of the chronic cases.

The findings in the author's 18 cases were similar. Only 6 of the patients had farming connexions. The response to the intradermal brucellergin test was uni-

formly positive, while the response to the agglutination test was positive in 15 cases, the titre varying from 1 in 20 to 1 in 2,560 (mean 1 in 130). The results obtained with brucellin and antibiotics in the treatment of chronic cases were poor, but there was apparent recovery in 7 out of 9 patients given capsules of a cobalt–copper–manganese preparation, each capsule containing 37 mg. of cobalt carbonate, 14 mg. of cupric sulphate, and 23 mg. of manganese carbonate, and the dosage being one capsule three times a day after meals. The author states that this dosage was given for 6 weeks and that after a rest period of 3 weeks administration was resumed and continued in this intermittent way for a year. In his view no single test is specific in the diagnosis of brucellosis; repeated laboratory and clinical observations over a period of months are often necessary.

[This is a rather rambling and disjointed paper.]

I. M. Librach

1217. **Pulmonary Nocardiosis. A Review with a Report of Seven Cases**

B. H. WEBSTER. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 485–500, April, 1956. 7 figs., 44 refs.

Pulmonary nocardiosis is an infection of the lung by *Nocardia*, an aerobic fungus of the family *Actinomycetaceae*, which was first reported in man in 1891 and of which the present author has been able to trace only 44 cases in the literature. The disease runs a variable febrile course, and the radiological appearances are similar to those seen in any infectious granuloma. The lower lobes are most commonly affected. Diagnosis is made by demonstrating *Nocardia* in the sputum by special stains and cultures. The fungus has the ability to produce acid-fast rods from its filaments, so that the microorganisms are easily confused with tubercule bacilli. There is usually a marked leucocytosis, and this may help in differentiating the disease from pulmonary tuberculosis. Treatment with sulphadiazine is often effective in early cases, or it may be combined with advantage with penicillin or tetracycline; in advanced cases surgical drainage or resection may be required. In the present paper details of 7 new cases, all of them due to *Nocardia asteroides*, are presented, thus bringing the total of published cases up to 51.

C. M. Fletcher

1218. **Coccidioidomycosis. A Review and Presentation of 100 Consecutively Hospitalized Patients**

D. J. O'LEARY and F. J. CURRY. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 501–518, April, 1956. 11 figs., 30 refs.

The authors present an analysis of 100 consecutive patients with coccidioidomycosis seen at the Fitzsimons Army Hospital, Denver, Colorado, between October, 1948, and March, 1955. There were 4 fatal disseminated cases, 3 of which occurred in negroes, although there were only 11 negro patients in the whole series. Cough and chest pain were the commonest symptoms, and haemoptysis occurred in 18 cases. The radiographic signs were predominantly cavitary in 56 and nodular in 34; the abnormalities usually cleared in 2 to 6 weeks, but in several cases persisted for 2 or 3 months. Skin tests with coccidioidin were performed in 96 cases and gave a positive result in 71, positive reactions to histoplasmin were obtained in 27 cases, and serological tests gave positive results in 27 out of 70 cases tested. *Coccidioides immitis* was isolated in 41 out of the 91 cases in which cultural studies were carried out, most of these cases being of the cavitary type. There is no specific therapy other than resection, which was performed in 62 of the present cases. The pathology in these cases is briefly reported.

C. M. Fletcher

1219. **Staphylococcal Infection of the Lower Respiratory Tract in Adults with Influenza**

A. D. EVANS and M. EVANS. *Lancet* [*Lancet*] **1**, 771–774, May 26, 1956. 18 refs.

During the course of an influenza-A epidemic in 1953 4 out of 70 patients with pneumonia admitted to Cardiff Royal Infirmary were found to have coagulase-positive *Staphylococcus aureus* in the sputum in large numbers; all 4 patients were severely ill and 2 died. In each case evidence was obtained, either by isolating the virus or by finding rising titres in the complement-fixation test, that there was coincident infection with influenza A. It was decided to investigate the level of circulating antibody to the α haemolysin of the staphylococcus, which in healthy persons ranges from 0·2 to 2 units per ml.

In the 4 cases under consideration no antibody could be demonstrated, a result in contrast with the finding of normal levels in a large number of sera from other patients with respiratory infections, staphylococcal skin infections, and severe non-respiratory staphylococcal lesions. The authors consider that the circulating antibody may have been neutralized by the toxin produced as a result of the massive staphylococcal infection of the respiratory tract combined with the presence of an influenzal infection, and suggest that, in addition to antibiotics, staphylococcal antitoxin might be useful in the treatment of such cases if given at an early stage and in adequate dosage.

K. C. Robinson

1220. **Long-term Oxytetracycline (Terramycin) Therapy in Advanced Chronic Respiratory Infections**

W. H. HELM, J. R. MAY, and J. L. LIVINGSTONE. *Lancet* [*Lancet*] **1**, 775–777, May 26, 1956. 2 refs.

Further to their previous report on the effect of long-term oxytetracycline therapy in advanced chronic respiratory infections (*Lancet*, 1954, **2**, 630; *Abstracts of World Medicine*, 1955, **17**, 128) the authors now present a follow-up report from the Brompton Hospital, London, on 8 patients who have now been receiving this treatment with benefit for periods ranging from $1\frac{1}{2}$ to $2\frac{3}{4}$ years. At the beginning of the investigation there were 38 patients, but for various reasons treatment was continued in only 14, and of these one (a child with chronic staphylococcal pneumonia) died after 3 years, one developed severe diarrhoea, 2 derived only slight benefit, and in 2 it was abandoned in favour of an autogenous vaccine. Of the remaining 8, which form the subject

of this report, 5 have chronic bronchitis and 3 bronchiectasis; the dose of oxytetracycline has varied from 1 to 3 g. daily. In all cases sputum has been reduced in quantity; *Haemophilus influenzae* has been isolated intermittently, but in only one patient was this organism resistant to the antibiotic. In one case a patient's sputum has persistently contained *Proteus vulgaris* and in another *Pseudomonas aeruginosa* but without any apparent harmful effects.

It was found more difficult to secure a good result if treatment was interrupted, and the authors consider that *H. influenzae*, which was the original infecting organism in most cases, has been suppressed but not eradicated; this organism appears to develop resistance very slowly. The study has also shown that recurrent pneumococcal infections, which are otherwise so common in these patients, are completely prevented. How long treatment can be continued with benefit remains uncertain.

K. C. Robinson

1221. **Primary Atypical Nonbacterial Pneumonia. An Evaluation of the Efficacy of Antibiotic Therapy in One Hundred Eighteen Cases**
R. L. Wolf and L. T. Brown. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 593–598, May, 1956. 18 refs.

Four groups of patients with primary atypical nonbacterial pneumonia were treated with chlortetracycline [aureomycin], erythromycin stearate, oxytetracycline hydrochloride, and tetracycline hydrochloride, respectively. These patients were compared with a control group of patients with primary atypical nonbacterial pneumonia who received no specific therapy. The results indicate that the antibiotics employed do not alter the duration of pneumonitis in primary atypical nonbacterial pneumonia.—[Authors' summary.]

1222. **Biomycin in the Treatment of Patients with Suppurative Diseases of the Lungs.** (Лечение больных нагноительными заболеваниями легких биомицином)
R. A. Aksyanova. *Советская Медицина* [*Sovetsk. Med.*] 8–13, No. 4, April, 1956. 2 figs., 1 ref.

Of 20 patients with suppurative disease of the lungs who were treated with " biomycin " at the Stalin Second Institute of Medicine, Moscow, 4 had acute lung abscess, 13 chronic pneumonia with bronchiectasis and fibrosis, and 3 chronic bronchitis with bronchiectasis, emphysema, and fibrosis with manifestations of cardiopulmonary insufficiency. All were producing large amounts of purulent sputum and all had pyrexia with signs of toxaemia, leucocytosis, and a raised erythrocyte sedimentation rate. Bacteriological examination of specimens of sputum from each patient revealed staphylococci, streptococci, Gram-positive and Gram-negative rods, and Gram-negative intestinal organisms, alone or in various combinations. All these organisms were shown to be susceptible to biomycin in concentrations of 0·007 to 0·5 μg. per ml.

Biomycin was given orally in doses of 0·2 g. 6 to 8 times in the 24 hours, depending on the severity of the illness. A course lasted 7 to 14 days and was repeated in 17 patients after an interval of 10 to 20 days. After the ingestion of 0·2 g. of the antibiotic the following blood concentrations were reached: at 1 hour 0·5 to 2 μg. per ml., at 3 hours 1·6 to 4·6 μg. per ml., and at 5 hours 0·9 to 2·3 μg. per ml., while in the sputum the maximum concentration (0·4 to 2·2 μg. per ml.) was achieved at the end of 3 hours, falling at 5 hours to 0·05 to 0·09 μg. per ml. If the dose of biomycin was increased to 0·4 g., then the blood concentrations were: at 1 hour 7 μg. per ml., and at 3 hours 5·76 to 7·7 μg. per ml., while the sputum concentration reached in 3 hours was 0·3 to 4·0 μg. per ml. Thus in every case it was possible to achieve effective concentrations of the antibiotic both in the blood and in the sputum.

Clinically, all 20 patients were improved by the treatment, although the best results were obtained in the 4 patients with acute suppurative lesions (of one to 2 months' duration). Side-effects were not serious, 5 patients experiencing some degree of nausea, which passed off in 4 cases after an interruption of treatment for 12 hours, while in only one case had the treatment to be withdrawn, after 6 days, because of nausea and vomiting.

Marcel Malden

1223. **Neomycin Aerosol in the Pulmonary Complication of Cystic Fibrosis of the Pancreas**
G. E. Gibbs and J. Raskin. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 332–336, May, 1956. 1 ref.

The bacterial infection in the " chronic bronchitis " of children with cystic fibrosis of the pancreas has hitherto proved difficult to control because the causative organisms develop resistance to the antibiotics commonly employed at present. However, few, if any, bacterial strains resistant to neomycin are to be expected as this antibiotic is not widely useded. On the other hand in respiratory as distinct from surface infections this agent must be given by aerosol spray since ototoxic and nephrotoxic side-effects frequently accompany parenteral administration.

In preliminary trials small doses of neomycin, 8 to 16 mg. per kg. body weight per day, given by inhalation to 6 infants aged 18 to 24 months suffering from cystic disease of the pancreas with the usual pulmonary complications resulted in an appreciable reduction in the leucocyte count in all except one infant. In further preliminary tests the blood level after inhalation of the aerosol for 10 minutes to give a dosage of 17 to 50 mg. per kg. body weight was found to be in the region of 1·3 to 2·5 μg. per ml. This corresponds to the blood level obtained after parenteral administration of the drug which sometimes gave rise to toxic side-effects.

A dosage of 50 to 70 mg. per kg. per day was then adopted as the standard for trial in 3 advanced cases of cystic fibrosis of the pancreas with pyogenic staphylococcal infection of the bronchi. In 2 of the patients, a 10-year-old boy and a 7-month-old girl, neomycin aerosol controlled the infection during the period of treatment and brought about a 50% reduction in the leucocyte count. The third patient, a 7-year-old girl, did not improve and there was no decrease in the leucocyte count at any time.

K. Zinnemann

Endocrinology

1224. **Endocrine Aspects of Argentaffinoma with Special Reference to the Use of Urinary 5-Hydroxyindoleacetic Acid Estimations in Diagnosis**
P. S. MACFARLANE, C. E. DALGLIESH, R. W. DUTTON, B. LENNOX, L. M. NYHUS, and A. N. SMITH. *Scottish Medical Journal* [*Scot. med. J.*] **1**, 148–155, April, 1956. 32 refs.

It is known that argentaffinomata contain 5-hydroxytryptamine, that in patients with argentaffinoma the level of 5-hydroxytryptamine in the blood rises, and that the compound is excreted in the urine as 5-hydroxyindoleacetic acid (5-HIAA). In this paper from the Western Infirmary, Glasgow, and the Postgraduate Medical School of London a method of estimating the urinary excretion of 5-HIAA is described and results of its determination in 12 cases of histologically proved argentaffinoma and 5 in which the diagnosis was uncertain are reported. In 5 cases in which it was known that the tumour had not been eradicated at operation the excretion of 5-HIAA was abnormally high, being from 3 to about 50 times the normal. The clinical signs were inconstant in all but one of these 5 cases. In 5 cases in which the clinical picture was inconclusive the urinary excretion of 5-HIAA was normal. Of the remaining 7 cases, excretion of the metabolite was normal in 6 in which there had been successful eradication of the tumour, but in the remaining case, where the tumour had been excised 9 years previously, the excretion was high and confirmed somewhat doubtful clinical evidence of recurrence.

P. A. Nasmyth

THYROID GLAND

1225. **A Radioiodine Uptake Test and Its Application in Clinical Diagnosis**
F. F. RUNDLE, W. A. SELDON, and J. S. INDYK. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 732–736, May 5, 1956. 6 figs., 20 refs.

In this paper from the Royal North Shore Hospital, Sydney, the authors describe a test of thyroid function based on the amount of radioactive iodine (^{131}I) accumulating in the thyroid gland within one hour of intravenous injection of a tracer dose. Thyroid uptake was measured as the ratio of the uptake in the neck to that in the thigh (the N:T ratio). The ^{131}I was given intravenously in a dose of approximately 10 millicuries and counts over the neck and thigh carried out exactly one hour after the injection. Since the N:T ratio only was used, it was not necessary to know exactly the amount of ^{131}I injected. The simple apparatus required is briefly described.

The test was carried out on 135 occasions on 121 patients, of whom 43 had various forms of simple goitre, 32 suffered from anxiety states, 10 had definite thyrotoxicosis, and 27 suffered from miscellaneous related conditions, though none of them was clinically thyrotoxic [a total of only 112 cases]. In the patients with non-toxic goitre the N:T ratio ranged from 0·4 to 3·8, those with anxiety states from 0·4 to 3·0, in the thyrotoxic patients from 5·5 to 52·0, and in the miscellaneous group was less than 4 in every case. The N:T ratio correlated well with the basal metabolic rate in thyrotoxic patients but not in those with anxiety states.

From consideration of the results in these four groups it would appear that the approximate upper limit of normal for the N:T ratio as measured by this test is 4. However, as this ratio represents uptake of iodine by the thyroid and not the discharge of hormone from the gland, and as these two functions do not always run in parallel, it follows that such a dissociation when it occurs may be a source of diagnostic error in the test. Clinically, it may appear, for example, as the result of the use of thyroid blocking agents. The authors suggest that the chief clinical value of the test lies in allowing a rapid separation of patients with thyrotoxicosis from those with anxiety states. It might also be of help in the study of cardiac failure with suspected hyperthyroidism when dyspnoea interferes with the accurate determination of the basal metabolic rate.

Marcel Malden

1226. **A Statistical Appraisal of the Serum Protein-bound Iodine as a Test of Thyroid Function**
M. E. DAILEY and J. R. SKAHEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 907–909, May 10, 1956. 2 figs., 7 refs.

The purpose of this study was to assess statistically the value of the serum protein-bound iodine concentration as an indicator of thyroid function, the data consisting of the records of a consecutive series of patients seen at the Veterans Administration Hospital, Oakland, California, for whom figures for this value were available. The patients were classified as euthyroid, hypothyroid, or hyperthyroid by clinicians without knowledge of these figures, but with reference to all other available clinical and laboratory findings regarding thyroid function, including in every case the basal metabolic rate. The following were excluded from the study: (1) patients whose records included no definite statement about thyroid function; (2) patients who at any time had taken organic iodine compounds or who within 2 months had taken inorganic iodine; (3) patients with known endocrinopathy apart from thyroid disorders; and (4) patients who were pregnant.

The homogeneity of the euthyroid group (804 cases) was examined by comparing the frequency distributions and the mean values for serum protein-bound iodine concentration among seven sub-groups, which are described in detail in the paper. They were briefly as

follows: (1) 313 controls, consisting of 250 female and 63 male patients with no history of thyroid dysfunction; (2) 126 patients in whom a psychiatrist had diagnosed an anxiety state, but who had no thyroid dysfunction; (3) 44 grossly overweight patients; (4) 96 with an enlarged and palpable thyroid gland; (5) 141 who had undergone thyroidectomy; (6) 49 who had been treated with radioactive iodine; and (7) 35 who were receiving thyroid extract to maintain a euthyroid state. The authors state that " statistical analysis established their (the seven groups) homogeneity ". [Details of the analysis are not given, but histograms of the distributions are shown together with the mean values; for example, the mean for female control subjects is given as $6{\cdot}19 \pm 1{\cdot}09$ μg. per 100 ml., but it seems likely from the histograms that 1·09 is not the standard error of the mean, as might be expected from conventional usage, but the standard deviation of the distribution. If so, then the sub-group of overweight patients probably had a significantly (at $P=0{\cdot}05$) lower mean value than the other sub-groups.] Among the 313 controls there was no evidence of a sex difference or correlation with age ($r=-0{\cdot}1$) in regard to the serum protein-bound iodine concentration.

The euthyroid, hyperthyroid, and hypothyroid groups were then compared by use of the cumulative frequency distributions and mean values for concentration of serum protein-bound iodine. [The results given below are derived only from notes on the diagrams of the frequency distributions. From these it appears that only the 313 controls were used to represent the euthyroid group. As the test of homogeneity was made on the whole group of 804 euthyroid patients and the authors were satisfied on this score, it may well be that in fact the distribution and mean shown on the diagram refer to the total number of 804 patients. Unfortunately, from the meagre information available, the mean quoted for this group cannot be reconciled either with the means for male and female subjects among the 313 controls or with the means of the sub-groups of the 804 patients.] The mean results for the serum protein-bound iodne concentration, in μg. per 100 ml., were as follows:

	No. of Patients	Mean	σ
Hypothyroid	63	3·58	1·10
Euthyroid	313	6·16	1·49
Hyperthyroid	258	11·44	3·14

[The text implies that σ=standard error of the mean, and the significance of the difference between means would appear to be assessed on this basis; but again the distributions suggest that, in fact, σ=standard deviation of the distribution.] The authors conclude that there was a significant difference between the hyperthyroid and hypothyroid groups ($P<0{\cdot}01$) and between the hyperthyroid and euthyroid groups ($P<0{\cdot}05$), but that there was no significant difference between hypothyroid and euthyroid. [If the above opinion about σ is correct, then of course all three differences are highly unlikely to have occurred by chance, a result which adds weight to the authors' final conclusion.]

About 75% of the cases in the hyperthyroid group had concentrations in excess of the maximum in the euthyroid group, and the authors conclude that " the greatest value of the test is that elevated values of protein-bound iodine in the absence of pregnancy, thyroiditis or iodine medication make the diagnosis of hyperthyroidism highly probable ".

E. A. Cheeseman

1227. **The Serum Protein-bound Iodine during Treatment of Thyroid Disorders.** [In English]
P. WAHLBERG, B. A. LAMBERG, and P. I. FORSIUS. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 257–265, May 26, 1956. 3 figs., 14 refs.

At the University and the State Serum Institute, Helsinki, the authors have studied the behaviour of the serum protein-bound iodine (S.P.I.) in patients with (1) thyrotoxicosis treated surgically (54 cases) or with antithyroid drugs (31 cases); (2) non-toxic nodular goitre treated surgically (11 cases); and (3) myxoedema treated with thyroid (14 cases).

They found that after operation (subtotal thyroidectomy) for thyrotoxicosis there was a general tendency for the S.P.I. level to fall; in some cases the abnormally low levels enabled them to detect postoperative hypothyroidism as early as 2 months after operation. In the one case of recurrence in the series the S.P.I. level rose. In thyrotoxic patients treated with antithyroid drugs there was some correlation between the S.P.I. level and the clinical state or the correctness of dosage. Although the S.P.I. level rose considerably after treatment in some hypothyroid cases, this rise was not constant, and the authors consider the clinical state of the patient to be the most important guide to treatment. After removal of a non-toxic nodular goitre the S.P.I. level usually remained constant or fell, though in a number of cases a marked rise occurred. This last finding seems to confirm a previous report of a marked change in thyroid function taking place after such an operation (*Acta endocr.* (*Kbh.*), 1950, **5**, 249).

The authors conclude that estimation of S.P.I. content " is a valuable aid in the evaluation of the postoperative course in thyrotoxicosis, especially in finding early signs of postoperative hypothyroidism ".

J. Warwick Buckler

1228. **Treatment of Thyrotoxicosis with Radioactive Iodine (I^{131}).** [In English]
B. C. CHRISTENSEN, V. DAHL, K. B. PETERSEN, and B. STRANGE. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 275–288, May 26, 1956. 2 figs., 38 refs.

In this paper from the Finsen Memorial Hospital, Copenhagen, the authors review some of the published accounts of the treatment of thyrotoxicosis with radioactive iodine (^{131}I) and survey the biological and physical properties of the isotope They narrow down the indications for its use to: " (1) complicating heart disease; (2) high age [apparently over 45 years, unless other criteria apply]; (3) previous strumectomy; (4) very large

intrathoracic goitre; and (5) the few cases where, despite adequate treatment, it has been impossible to bring the patient into an operative state" [which they regard as optimal]. They have adopted these criteria in selecting the 45 cases whose treatment they now describe. An average dose of 5·85 mc. of ^{131}I per treatment was given. The number of treatments varied according to individual requirement, only one dose being needed in 37 cases to obtain euthyroidism. The progress of the disease was evaluated clinically and by serial measurements of weight and basal metabolic rate. All patients were followed up for at least 6 months, the majority for up to 2 years. Of the 45 patients, 34 were cured, 5 were improved, 3 became myxoedematous, 2 were unchanged, and one died from myocardial infarction after a thyroid crisis.

The authors express the view that in these cases of thyrotoxicosis the risk of secondary development of cancer will not be known for at least 15 years, nor can gene damage be precluded, though this risk is small. They compare the results of treatment with radioactive iodine in their own series with these in other series treated with radioactive iodine, operation, or antithyroid drugs. *J. Warwick Buckler*

1229. **Therapeutic Activity of Desiccated Thyroid Substance, Sodium L-Thyroxine and DL-Triiodothyronine. A Comparative Study**
T. H. McGavack and H. K. Reckendorf. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 774–777, May, 1956. 24 refs.

A comparative investigation is reported of three thyroid preparations in the treatment of 12 patients with the classic signs and symptoms of myxoedema, the diagnosis being confirmed by the results of determination of the basal metabolic rate (B.M.R.) and of the thyroid uptake of radioactive iodine. The procedure was as follows: each patient was brought to a euthyroid state by administration of desiccated thyroid, or sodium L-thyroxine, or DL-triiodothyronine, and then allowed to revert to a hypothyroid state, with a B.M.R. of −20% or below; this was followed by a further period of treatment with another thyroid preparation. Altogether 60 trials were completed over a period of 3 years.

It was found that 60 mg. of desiccated thyroid was equivalent in activity to 100 μg. of sodium L-thyroxine and to 60 μg. of DL-triiodothyronine. The average optimum daily dose of desiccated thyroid was 120 to 180 mg., that of sodium L-thyroxine was 200 to 350 μg., and that of triiodothyronine was 60 μg. Administration of DL-triiodothyronine restored a euthyroid state in an average of 5 days, compared with 19·2 days for sodium L-thyroxine and 21 days for desiccated thyroid. However, angina was a more frequent side-effect after DL-triiodothyronine than after the other two preparations. *I. McLean Baird*

1230. **Fatal Marrow Aplasia after Treatment with Carbimazole**
C. D. Burrell. *British Medical Journal* [*Brit. med. J.*] 1, 1456–1457, June 23, 1956. 7 refs.

PANCREAS

1231. **Relation of Glucagon to α Cells of the Pancreas**
S. A. Bencosme and J. Frei. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 589–592, April, 1956. 3 figs., 17 refs.

The authors, at Queen's University, Kingston, Ontario, have attempted to locate the site of production of the hyperglycaemic–glycogenolytic factor (glucagon) in the pancreas of the guinea-pig. The animals received injections of cobalt chloride, which causes a progressive degranulation of the α cells of the pancreas. The extent of the α-cell lesion was graded histologically on the basis of the proportion of the α cells in the pancreas showing complete degranulation, as follows: 1+, some degranulated cells observed; 2+, about half the α cells degranulated; and 4+, only a few granulated α cells remaining.

Pancreatic extracts from these animals were tested for their hyperglycaemic effect on fasting anaesthetized cats, and it was found that extracts from animals having 1+ or 2+ lesions elicited a response similar to that of extracts from untreated animals, whereas those from animals with 4+ lesions had no hyperglycaemic effect. In the authors' view these results strongly suggest that glucagon is elaborated in the α cells of the pancreas. The absence of an extractable hyperglycaemic factor, presumably glucagon, was associated only with a 4+ lesion, which occurred in about 40% of the animals. It is suggested that the conflicting results obtained by other workers may have been due to failure to grade the extent of the pancreatic lesion. *M. J. H. Smith*

1232. **Glucagon and the Regulation of Carbohydrate Metabolism**
H. Elrick. *Nature* [*Nature (Lond.)*] **177**, 892–893, May 12, 1956. 1 fig., 11 refs.

There is considerable evidence that glucagon (hyperglycaemic factor of the pancreas), which was isolated and crystallized in 1953, is a true hormone secreted by the α cells of the islets of Langerhans. Minute doses of crystalline glucagon cause a significant rise in the blood sugar level, which is probably brought about by a stimulation of liver glycogenolysis, although the exact mechanism is not known.

The present author, from the Veterans Administration Hospital and University of Colorado Medical School, Denver, reports the results of experiments on 56 healthy males in which the effects of glucagon and/or insulin on arterial and venous blood sugar levels were studied for 60 to 110 minutes following a control period of 30 to 60 minutes during which glucose alone was infused. It was found that glucagon caused a highly significant increase in the difference between arterial and venous blood glucose levels. Insulin also increased the arterial–venous blood glucose difference. When insulin and glucagon were given together the differences between arterial and venous glucose levels were significantly greater than when either insulin or glucagon was given alone.

These findings suggest that glucagon has a dual action —namely, it promotes the release of liver glycogen and enhances peripheral glucose utilization. They also suggest that glucagon and insulin may function together to accelerate the peripheral utilization of glucose. The two hormones have opposing actions on the blood glucose and liver glycogen levels, so that each may complement the effect of the other in maintaining these two reservoirs of body glucose constant in the face of an accelerated rate of utilization of peripheral glucose. The mechanism is not clear, but it is probable that the liver is necessary for enhancing the effect of glucagon on peripheral glucose utilization. *John Lister*

1233. **The Effect of Glucagon on Carbohydrate Metabolism in Normal Human Beings**
P. K. BONDY and L. R. CARDILLO. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 494–501, May, 1956. 43 refs.

Since the demonstration that a hyperglycaemic factor, glucagon, is released from the pancreas into the blood stream, the possibility that diabetes mellitus might result from an imbalance between the secretion of insulin and glucagon has been the subject of much speculation. However, from the results of experiments *in vitro* it would seem that glucagon produces a rise in the blood sugar level not by an inhibition of glucose utilization in the peripheral tissues, but merely by activating glycogenolysis in the liver.

In experiments carried out at Yale University School of Medicine the effect on the arterial and venous blood sugar levels of an injection of glucagon, with or without glucose, into healthy human subjects was studied, blood samples being taken before and at frequent intervals for 15 minutes after the injection. There was no evidence of reduced glucose utilization and it is suggested that glucagon may be regarded as working synergistically with insulin rather than counteracting its action, its function being to release glucose from the liver and thus make it available for the peripheral utilization which is promoted by insulin. *H. Lehmann*

1234. **Clinical Correlates of the Kimmelstiel–Wilson Lesion**
F. H. EPSTEIN and V. J. ZUPA. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 896–900, May 10, 1956. 1 fig., 19 refs.

An investigation was carried out to determine whether there were any differences between the clinical course of diabetes accompanied by nodular intercapillary glomerulosclerosis and that of diabetes without this complication. Out of 137 diabetic patients coming to necropsy at New Haven Hospital, Connecticut, between 1944 and 1953, 37 had nodular glomerular lesions in the kidneys, and the case records of these (Group 1) were analysed and compared with those of 37 controls (Group 2) selected at random from the remainder. Pyelonephritis was present in 28 cases in Group 1, compared with 8 in Group 2, while arteriosclerosis was found in all the cases in Group 1 but in only 7 in Group 2. The clinical findings in Group 1 (with the corresponding figures for Group 2 in brackets) were as follows: persistent albuminuria in 32 (2) cases, hypoproteinaemia in 22 (7), oedema in 30 (12), a raised serum non-protein nitrogen level in 22 (3), and retinopathy in 30 (9). The average age of the Group-1 patients at death was 55 years, compared with 60 years in Group 2, and the duration of diabetes was 14 years in the former and 9 years in the latter group. Hypertension and neuropathy were more frequent in Group 1 (30 and 20 cases respectively) than in Group 2 (23 and 13 cases). The insulin requirements had been similar in the two groups, and also the incidence of acidosis. It would appear that a clinical diagnosis of nodular glomerulosclerosis can be based on the simultaneous finding of persistent albuminuria, hypertension, retinopathy and neuropathy, cardiac failure, and renal failure in elderly diabetics. *L. H. Worth*

1235. **Blood Groups in Diabetes Mellitus**
R. B. MCCONNELL, D. A. PYKE, and J. A. F. ROBERTS. *British Medical Journal* [*Brit. med. J.*] **1**, 772–776, April 7, 1956. 12 refs.

The results are reported of two independent investigations carried out in Liverpool and Oxford into the incidence of ABO blood groups in 1,333 patients suffering from diabetes (833 at the David Lewis Northern Hospital, Liverpool, and 500 at the Radcliffe Infirmary, Oxford) and in healthy controls from the general population. Because of certain variations in the distribution of blood groups among controls in the Liverpool area the entire material was divided into three series, covering respectively south-west Lancashire, west Cheshire, and Oxford.

The proportion of male diabetics with Group-A blood was high compared with male controls, the difference being highly significant by the χ^2 test and homogeneous in all three series. No significant difference was observed in blood group distribution between the female diabetics and controls. The authors point out that their findings do not support those of Craig and Wang (*Glasg. med. J.*, 1955, **36**, 261), who, in a similar investigation among diabetics at the Victoria Infirmary, Glasgow, did not observe any significant difference between diabetics and controls in the incidence of ABO blood groups. *I. McLean Baird*

1236. **Parity and the Incidence of Diabetes**
D. A. PYKE. *Lancet* [*Lancet*] **1**, 818–821, June 2, 1956. 3 figs., 11 refs.

The effect of parity and of weight on the incidence of diabetes was studied in 953 patients (583 females and 370 males) attending a diabetic clinic at the Radcliffe Infirmary, Oxford. The investigation showed that over the age of 45 the incidence of diabetes was higher in females than in males, the excess over the expected incidence being confined to women who had borne children and rising with each degree of parity. The author states that although the multiparae tended to be overweight, this factor alone was not sufficient to explain the high incidence of diabetes mellitus among the higher parity groups. The degree of parity did not appear to influence the age at onset of the diabetes.

[This study confirms a well-established clinical impression. Although the relatively large number of patients makes the conclusions fairly reliable, it should be noted that the criteria for the diagnosis of diabetes are not stated.] *J. N. Harris-Jones*

1237. **Foetal Mortality in Pregnant Diabetics. Strict Control of Diabetes with Conservative Obstetric Management**

J. PEDERSEN and E. BRANDSTRUP. *Lancet* [*Lancet*] 1, 607–610, May 5, 1956. 13 refs.

In a report from Rigshospitalet, Copenhagen, the authors discuss the foetal mortality in 265 pregnancies in diabetic women seen during the period 1946–55, a series of 157 such cases admitted in the years 1926–45 being used for comparison. Since January, 1946, the routine management has consisted in strict control of the diabetes and conservative obstetrical measures. Women with diabetes are admitted 8 weeks before expected term and remain in hospital until delivery; labour is induced, on an average, 20 days before term, in most cases by means of drugs and/or by rupture of the membranes. Delivery was by Caesarean section in 29 cases (11%). In about 20% of the 265 cases labour started spontaneously.

For the purpose of the present study the patients were divided into two groups according to the stage of pregnancy at which they first sought advice. Those seen at least 53 days before term were classified as "long-term treated" (130 cases; Group 1), and those seen later as "short-term treated" (135 cases; Group 2). In Group-1 cases the foetal mortality was 10%, as compared with 33% in Group 2. The over-all foetal mortality in the period 1926–45 was 38%. In the 113 cases seen during the last 3 years of the study (1953–5) the total foetal mortality was 15%, the figure for the 72 cases belonging to Group 1 being only 8%. Caesarean section was performed in 17 (15%) of these 113 cases.

The authors state their opinion that in cases of diabetes in pregnancy "it is unnecessary to give sex hormones or to do many Caesarean sections". They also emphasize the importance of long-term treatment, and of "one-physician close supervision" during the last months of pregnancy, in reducing the foetal mortality.

A. I. Suchett-Kaye

1238. **Insulin–Zinc Suspensions. Further Studies, with Emphasis on Lente Insulin**

J. L. IZZO. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 554–563, April, 1956. 8 figs., 12 refs.

The author reports, from the Strong Memorial and Municipal Hospitals, Rochester, New York, the results of a clinical comparative study of insulin zinc suspension (a mixture consisting of 70% suspended in the crystalline form and 30% in the amorphous form) with NPH (isophane) insulin in which 6 patients with severe unstable diabetes took part. Each patient was kept on a constant weighed diet and received a single daily injection of insulin given before breakfast, each type of insulin being given alternately for successive periods of 4 or 5 days, the effect on the blood sugar level and the degree of glycosuria being compared. Variability of the blood sugar level during a single day and from day to day was much the same with both types of insulin, showing that they were similar in regard to the predictability and consistency of their action. Comparison of the patterns of variation of the blood sugar level throughout the day indicated that the action of insulin zinc suspension was on the whole similar to, but very slightly slower than, that of isophane insulin, although there were some striking differences in individual cases; for example, in 4 cases in which NPH insulin acted strongly during the afternoon and evening but allowed high levels of blood sugar at night and in the morning insulin zinc suspension produced a more even pattern of response. In contrast, in cases in which isophane insulin produces high blood sugar levels during the day and lower levels at night, insulin zinc suspension may exaggerate the pattern.

A study was carried out *in vitro* of the solubility in human serum of amorphous insulin zinc suspension, crystalline insulin zinc suspension, and mixtures of the two. The solubility curves obtained, taken together with the available clinical evidence, suggested that it is possible to obtain a range of insulin zinc suspensions with different durations of activity.

[Isophane insulin has been widely used and fully studied in the U.S.A., while in Western Europe attention has been concentrated on the insulin zinc suspensions (lente insulins). This authoritative paper provides an interesting comparison between these two types of insulin.] *K. O. Black*

1239. **Hypoglycemic Action of Sulfonylureas in Patients with Diabetes Mellitus**

I. A. MIRSKY, D. DIENGOTT, and H. DOLGER. *Science* [*Science*] **123**, 583–584, April 6, 1956. 2 figs., 4 refs.

After an overnight fast, the usual morning dose of soluble insulin was withheld from 44 adult diabetics, none of whom had received a long-acting insulin during the previous few days. Each was then given 1-butyl-3-*p*-tolylsulphonylurea ("orinase") by mouth in a dose of 50 mg. per kg. body weight as a 2% solution in 0·5% sodium bicarbonate solution adjusted to *p*H 8, the venous blood glucose levels being determined before, and at intervals for 5 hours after, ingestion of the drug. A control group of 24 diabetics were given 5 ml. of 0·5% sodium bicarbonate per kg., the same procedure being followed. Whereas a slight increase in the blood sugar level occurred in the control subjects, 34 of the 44 patients given the tolylsulphonylurea showed a hypoglycaemic response which was statistically highly significant. In the remaining 10 patients, all of whom had developed diabetes before the age of 20 and had suffered from it for at least 8 years, the response was absent or negligible, while in those who responded the degree of hypoglycaemia appeared to be directly related to the age at onset and also to the duration of the diabetes.

While their results confirm those of previous investigators, the authors consider that full assessment of the therapeutic usefulness of the sulphonylureas in diabetes must await extensive clinical trial, which should be

carried out with caution since these drugs appear to be non-competitive rather than competitive inhibitors of insulinase. *H.-J. B. Galbraith*

1240. **Orinase, a New Oral Hypoglycemic Compound**
W. L. MILLER and W. E. DULIN. *Science* [*Science*] **123**, 584–585, April 6, 1956. 2 figs., 7 refs.

" Orinase " (1-butyl-3-*p*-tolylsulphonylurea), given by mouth in a dose of 270 mg. per kg. body weight, produced a rapid and substantial decrease in the blood sugar level in fasting rats within half an hour. This effect was maintained for more than 6 hours after ingestion, but after 12 and 15 hours the blood sugar levels in the treated rats were slightly higher than in the controls. The glycogen content of the liver was increased and that of muscle unaltered in the treated animals as compared with the controls in specimens of the tissues taken 7 hours after administration of the drug. In contrast, insulin caused an increase in the muscle glycogen level but no consistent change in liver glycogen content, suggesting a difference in mechanism between the two drugs, whose effects can in turn be contrasted with that of " synthalin ", which produces a depression of the liver glycogen content.

The effects of orinase and its sodium salt on the blood sugar level of the starving dog were similar, except that the latter had a more rapid action, a single oral dose of 25 mg. per kg. maintaining the blood sugar content at 25% below the control level for over 24 hours. A dose of 100 mg. per kg. produced a greater and more prolonged hypoglycaemia, but a dose of 600 mg. per kg. had no further effect on the blood sugar level, although death followed within 20 hours. Rabbits required larger doses of orinase to produce similar degrees of hypoglycaemia, while its duration of action was very much shorter. Death followed the administration of about 3,500 mg. per kg., but again was not due to hypoglycaemia. Studies of the toxicity of the drug to various species on continued administration have shown no evidence of haematological disturbance, but a moderate-sized goitre developed in all rats which were given large doses. *H.-J. B. Galbraith*

1241. **Insulin-sparing Sulfonamides**
L. W. KINSELL, F. R. BROWN, R. W. FRISKEY, and G. D. MICHAELS. *Science* [*Science*] **123**, 585, April 6, 1956. 1 ref.

The treatment is reported of 10 patients, 5 with " severe ", 4 with " mild ", and one with " preclinical " diabetes, with the hypoglycaemic sulphonamides " BZ 55 " (N-butyl-N′-sulphanilylurea) or " orinase " (1-butyl-3-*p*-tolylsulphonylurea) by mouth in doses of 1 to 16 g. per day. In 3 severe cases the drugs had a definite hypoglycaemic or insulin-sparing action in daily doses of 2 g. or more, in one there was a significant increase in glycosuria, while in the fifth there was no response. The insulin requirements of 3 middle-aged, obese patients with mild diabetes were reduced by over one-half by the daily administration of less than 2 g. of sulphonamide, while in the other mild case a 50% reduction in blood sugar level occurred after a single dose of 3 g. In the case of " preclinical " diabetes the glucose tolerance curve, which was previously of the diabetic type, became normal after a single dose of 6 g. of sulphonamide.

During the intensive administration of the drugs to the 3 patients with severe diabetes who responded well the uptake of radioactive iodine by the thyroid was considerably reduced, but it reverted to normal with reduction in the dosage of sulphonamide. With very large doses of the sulphonamides a fall in the granulocyte count, with arrest of maturation in the bone marrow, was noted, but the blood count returned to normal after a reduction of dosage.

In 2 cases of severe juvenile diabetes all of the administered sulphonamide was excreted in the urine, but whereas in the urine of one patient who responded well to the drug the greater part of the sulphonamide was conjugated, in that of the other, whose glycosuria increased during treatment, it was mostly free.

H.-J. B. Galbraith

1242. **Therapeutic Trial in Diabetes Mellitus in Adults of Synthetic Hypoglycaemic Agents of the Sulphonamido-thiodiazol Group (2254 and 2261 RP).** (Essai de traitement du diabète sucré de l'adulte par des hypoglycémiants de synthèse de la série des sulfamido-thiodiazols (2254 et 2261 RP))
E. AZÉRAD. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **72**, 424–435, May 4, 1956. 5 refs.

The author presents the case records of 25 diabetic patients (13 women and 12 men, average age 53) who were treated with the sulphonamides *p*-aminobenzenesulphonamido-2-*iso*propyl-5-thiodiazol (" 2254 RP ") and *p*-aminobenzenesulphonamido-2-*n*-amyl-5-thiodiazol (" 2261 RP "). Of 7 patients aged 54 to 74 whose diabetes was at first mild and did not require insulin, 6 were well controlled by one or other of the two compounds, but the seventh patient required insulin as well. Of another group of 15 patients who were already receiving insulin treatment and some of whom were insulin-resistant, 3 could not tolerate the sulphonamide, 3 of the youngest were unaffected, but the 9 others benefited from treatment in that the dose of insulin necessary to control the diabetes could be reduced. (The substitution of " BZ 55 " (N-butyl-N′-sulphanilylurea) for insulin was associated with a severe acidosis in one of these patients). The improvement lasted only so long as the course of treatment was continued but the course could be successfully repeated.

In this series 4 patients were intolerant of 2261 RP and one of 2254 RP, 2 of them suffering from nausea and 2 becoming febrile during treatment, although in one of the latter the relationship of the fever to the therapy was not established, for it continued after withdrawal of the drug. In 2 cases there was a macular eruption which, however, did not prevent continuance of the treatment. A number of patients receiving 2261 RP complained of vague malaise, but treatment was not interrupted. The author considers that these sulphonamides are useful in the control of insulin-resistant diabetes in elderly patients, though they do not replace insulin. *H. E. Holling*

The Rheumatic Diseases

1243. **Landis's Test in the Diagnosis of Rheumatic Disorders.** (Il test di Landis in semeiotica reumatologica)
C. Cervini, F. S. Fragale, and C. Longo. *Minerva medica* [*Minerva med. (Torino)*] **1**, 1326–1330, May 2, 1956. 43 refs.

Landis's test as originally described in 1932 was an estimation of the capillary permeability after the production for 30 minutes of venous stasis with a sphygmomanometer cuff at various pressures, a full blood count, haematocrit reading, and determination of the plasma protein level being carried out. The present authors have simplified the technique and now measure only the erythrocyte sedimentation rate (E.S.R.) and plasma protein level. At the Institute of Rheumatology, University of Rome, they have employed this modified test in 8 cases of chronic inactive rheumatoid arthritis, 20 of active rheumatoid arthritis, 8 of ankylosing spondylitis, and in 10 healthy control subjects.

The E.S.R. was raised and the plasma protein level lowered in all the cases of active rheumatoid arthritis and in 7 of the 8 cases of ankylosing spondylitis, while one or other value was changed in the eighth case of ankylosing spondylitis and in 2 of the 8 cases of inactive rheumatoid arthritis; in the other arthritic patients the alteration in the values was " not notable ". [The results in the controls are not stated, and it is regrettable that in the case of the patients no actual figures are given.] From this study the authors conclude that such a test is of diagnostic value in the rheumatic disorders and is a pointer to the role of capillary permeability in the pathogenesis of these diseases. *David Friedberg*

1244. **Observations on the Use of Prednisone in Patients with Progressive Systemic Sclerosis (Diffuse Scleroderma)**
G. P. Rodnan, R. L. Black, A. J. Bollet, and J. J. Bunim. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 16–29, Jan., 1956. 6 figs., 17 refs.

The results obtained with cortisone and corticotrophin in the treatment of diffuse scleroderma have been generally regarded as disappointing. In this paper from the National Institutes of Health, Bethesda, Maryland, a trial of prednisone in 6 patients (4 females and 2 males) suffering from progressive symmetrical scleroderma is reported, the dosage of the drug being 20 to 30 mg. a day for uninterrupted periods of 6 weeks to 4½ months. In all the cases there was improvement in the skin, with lessening of pigmentation, swelling, and tightness, and peripheral vasomotor changes were less marked. The most favourable response was obtained in patients with polyarthritis. One patient with pulmonary involvement experienced relief of exertional dyspnoea. Gastrointestinal symptoms were not influenced. Facial rounding was noted in 4 patients, in 2 of whom acne developed. In the 4 females there was an increased growth of hair on the face and limbs. *E. W. Prosser Thomas*

1245. **The Clinical Significance of the L.E. Clot Test**
L. A. Brunsting, J. M. Stickney, G. L. Pease, and W. B. Reed. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 307–312, April, 1956. 5 figs., 9 refs.

The records of 112 patients whose blood, when tested at the Mayo Clinic in 1951 and 1952, gave a positive reaction to the L.E.-cell test, have been reviewed with the object of assessing the value of the test more fully. The patients were divided into three groups according to the clinical picture: (1) typical (42%); (2) partly typical (35%); and (3) frankly atypical (23%). In the last group weakly-positive responses to the L.E. test were the rule, and not infrequently only one such response was obtained on repeated testing. The average age of the patients in this group was 45 years (compared with 35 years for those in whom the clinical picture was typical) and rheumatoid arthritis was the chief complaint. Of the 25 patients in this group, 7 had died, but in none of these was there any evidence of systemic lupus erythematosus at necropsy. The authors conclude that when the result of the test is weakly positive its significance is uncertain. The test is a great aid in the diagnosis of systemic lupus erythematosus, but the results will " not serve for prognostic purposes ". *E. G. Rees*

ACUTE RHEUMATISM

1246. **Antistreptolysin Response in Acute Rheumatic Fever in Children**
E. J. Holborow and I. C. Isdale. *Lancet* [*Lancet*] **1**, 649–651, May 12, 1956. 4 figs., 11 refs.

It has been established that most patients with acute rheumatic fever show evidence of recent infection with β-haemolytic streptococci of Lancefield's Group A, and that such patients have a significantly greater antibody response than those with uncomplicated infections. It has further been shown that in infants and young children antibody response increases with age, and it has been suggested that this may be due to conditioning of the antibody-forming organs by repeated exposure to streptococcal antigens. This observation, together with the rarity of rheumatic fever in very young children, has been held to support the concept that sensitization to streptococci or their products is closely related to the pathogenesis of rheumatic fever. In an attempt to elucidate this problem the authors have estimated the antistreptolysin-O titre in 107 rheumatic children at the Canadian Red Cross Memorial Hospital, Taplow, Bucks. Only those children were chosen who were seen in their first attack of acute rheumatic fever within 4 weeks of the onset of symptoms and were under 12 years of age. The highest titre found within 4 weeks of admission was recorded for this survey. Simultaneous throat and nose swabs were examined for Group-A β-haemolytic streptococci, and previous upper respiratory-tract infections

noted. No age difference in the frequency of positive swabs or preceding upper respiratory-tract infections was found, but the 20 children who were under the age of 6 years showed a significantly lower frequency of raised antistreptolysin titres and a significantly lower mean titre than those over that age. This is regarded as indicating that the pathogenesis of rheumatic fever is not primarily related to sensitization to streptococci or to their products. *G. W. Csonka*

1247. **Changes in the Plasma Proteins and the Erythrocyte Sedimentation Rate at Various Stages of the Rheumatic Process in Children.** (Изменения белковых фракций крови и РОЭ в динамике ревматического процесса у детей)
E. N. Maksakova. *Педиатрия* [*Pediatrija*], 26–31, No. 2, March–April, 1956.

The author has determined the plasma protein pattern and the erythrocyte sedimentation rate (E.S.R.) in 100 children aged 4 to 13 years who were under treatment for acute rheumatism during the period 1951–4. For observation purposes the patients were divided into three groups as follows: (1) 24 patients with endocarditis and 5 without; (2) 9 with endocarditis and 27 with endo- or myocarditis; (3) 20 with diffuse myocarditis and 5 with pericarditis; all patients in this group had cardiac enlargement, tachycardia, and dyspnoea, and some also had rheumatic nodules, annular rashes, and polyserositis. The remaining 10 children were suffering from chorea without cardiac involvement.

The results showed that in all three main groups the total plasma protein content was within the normal range, although in Group 3 it was near the lower limit. In all groups the plasma globulin level was raised by 55 to 60%, particularly in Group 3, in which also the rise persisted longer. In Groups 1 and 2 the plasma gamma-globulin level was raised by 20 to 25% and in Group 3 by 25 to 30%. The E.S.R. in all groups was raised to 50 to 60 mm. per hour, the maximum sedimentation occurring in the first 15 to 30 minutes. The E.S.R., however, was not found to have any prognostic significance.

In the 10 children with rheumatic chorea but without cardiac involvement it was found that the changes occurring in the plasma proteins were insignificant.
Edward D. Fox

1248. **Clinical Experience with a New Serological Test for Rheumatic Endocarditis and a Consideration of the Pathogenesis of Rheumatic Heart Disease.** (Klinische Erfahrungen mit einer neuen serologischen Untersuchungsmethode bei rheumatischer Endocarditis und Betrachtung der Pathogenese rheumatischer Herzerkrankungen)
K. Polzer and C. Steffen. *Cardiologia* [*Cardiologia (Basel)*] **28**, 380–400, 1956. 1 fig., 33 refs.

As a contribution to the solution of the problem of the early diagnosis of rheumatic carditis, the authors describe an immunological test based on the experimental work of Cavelti (*Schweiz. med. Wschr.*, 1948, **78**, 83; *Abstracts of World Medicine*, 1948, **4**, 223). The latter showed that the intraperitoneal injection of killed streptococci and an emulsion of cardiac tissue in the rat and rabbit produced antibodies to heart tissue and also inflammatory changes such as myocarditis and endocarditis. Further, the serum of patients with polyarthritis and various collagen diseases has been shown to contain antibodies to a mixture of heart, muscle, and joint tissues, demonstrable by the indirect Coombs test.

In the present study, carrried out at Hanusch Hospital, Vienna, the authors therefore tested the serum of 52 patients for auto-antibodies to a preparation of heart tissue, using the Coombs test. Nearly all of 25 cases of clinically active rheumatic carditis gave a positive test result, but of 4 cases of bacterial endocarditis, only one showed a doubtfully positive reaction. Out of 9 cases of old rheumatic carditis, 3 showed a positive test result, whereas among 15 patients with various non-rheumatic ailments, in only one, a case of nephrolithiasis, was the reaction positive. The authors present a [somewhat elaborate] theory of the causation of rheumatic carditis, involving the formation of auto-antibodies.
G. Loewi

1249. **Natural Course of Active Rheumatic Carditis and Evaluation of Hormone Therapy**
M. G. Wilson and W. N. Lim. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1457–1460, April 28, 1956. 5 figs., 11 refs.

In an investigation at the New York Hospital–Cornell Medical Center of the effect of hormone therapy on the course of rheumatic carditis the history of 100 patients treated without hormones was compared with that of 55 receiving hormone therapy. The 100 control patients experienced 165 attacks of active carditis between 1930 and 1955. Their ages varied from 3 to 18 years; 72 of the attacks were initial and 93 recurrent. Careful study of the cases occurring in the two 10-year periods 1935–45 and 1945–55 showed that there had been no significant alteration in the type and severity of the disease. In one-fourth of the patients chorea and in one-half polyarthritis accompanied the carditis, and in about 12% of the attacks subcutaneous nodules were observed. The duration of active carditis was less than 2 months in 20% of the attacks, 2 to 4 months in 30%, and from 4 months to over a year in 50%. The follow-up period varied from 3 months to 21 years and averaged 9 years. During this time increase in cardiac physical signs rarely occurred without an obvious attack of carditis, and murmurs regressed in one-third of the patients.

The 55 patients (aged 4 to 19 years) receiving hormones were observed during 1949–55, and in all cases treatment was instituted within 3 to 21 days of onset. The attacks in 25 cases were initial and in 30 cases recurrent. The carditis in the hormone-treated group appeared to be slightly more severe than in the controls. The hormones used—corticotrophin, 25 units intramuscularly every 6 hours for 4 days and then 20 units 6-hourly for 3 days; cortisone, 100 mg. orally 6-hourly for 4 days and then 80 mg. 6-hourly for 3 days; and hydrocortisone, 80 mg.

6-hourly for 4 days and then 60 mg. 6-hourly for 3 days —were equally effective. In the majority of cases bradycardia developed on the 2nd day; transient hypertension was occasionally noted towards the end of treatment. In most cases heart size decreased and new murmurs regressed by the 3rd to 7th day. After therapy most cases in which treatment was started in the third week developed transient fever and joint pains on the 4th to 7th day, and in 3 cases evidence of carditis was observed, but this regressed spontaneously. The duration of active carditis was less than 2 months in all cases, in two-thirds of them being less than one month. It was found that the earlier therapy was started, the shorter was the duration of the carditis. While all the control patients had evidence of residual cardiac damage at the end of the attack, 84% of the hormone-treated group had no evidence of residual damage or, in the case of recurrent attacks, of an increase in residual cardiac damage. During the follow-up period of 6 months to 5 years murmurs regressed in two-thirds of the total group (as compared with one-third of the control patients).

In 8 additional cases receiving 7 days' hormone therapy one to 4 months after the onset of carditis there was no apparent effect on the disease. It is urged that it is essential that hormone therapy should be started as early in the course of the attack as is possible, while the lesions are still reversible. *C. Bruce Perry*

1250. **The Treatment of Chorea (General Management and Sleep Therapy).** (Лечение больных ревматической хореей)

B. L. Boverman. *Советская Медицина* [*Sovetsk. Med.*] 39–42, No. 4, April, 1956.

In this paper from the Bogomoletz Medical Institute, Kiev, the author describes his experience in the treatment of 28 cases of rheumatic chorea with a regimen of complete rest and prolonged sleep. The children were nursed in wards of 2 or 3 beds only, with shaded lights and isolated from noise, but well ventilated, in which a strict daily routine was observed, the time allowed for talking, playing, and reading being very limited. Once daily a teacher read or told the patients a story which was specially selected as being not likely to arouse any emotional tensions.

Drug therapy consisted of phenobarbitone, 0·02 to 0·05 g. twice a day, together with bromides and amidopyrine, 0·25 to 0·3 g. 4 times a day. The dose of phenobarbitone was usually decreased after the first 2 weeks, and in the majority of cases could be omitted after the 3rd week as the rhythm of spontaneous sleep developed. With these measures periods of prolonged sleep were easily achieved. Early in the investigation it was realized that 16 to 18 hours of sleep per day was too much, and thereafter the aim was 13 or 14 hours of sleep out of the 24, divided into 11 or 12 hours during the night and 2 or 3 during the day.

The results in the 28 children suffering from chorea of all degrees of severity who where treated by this method during 1951–2 are contrasted with those in a comparable group of 30 children treated in 1950 with the same drugs but without the regimen of prolonged sleep. The comparison showed that the addition of prolonged sleep shortened the duration of the illness and had a beneficial effect not only on the neurological and psychological manifestations of the illness, but also on the course of the cardiac complications. *Marcel Malden*

CHRONIC RHEUMATISM

1251. **Bone-marrow in Ankylosing Spondylitis**

E. M. K. Pillers and J. Marks. *Lancet* [*Lancet*] **1**, 722–723, May 19, 1956. 4 refs.

Patients with ankylosing spondylitis are said to be unusually susceptible to leukaemia. Since the literature does not contain a description of the bone-marrow findings before and after radiotherapy the present authors, in this paper from the University of Cambridge, report the results of bone-marrow examination in 28 patients with ankylosing spondylitis. Marrow hypercellularity was found in 5 of the 10 patients who had received one or more courses of irradiation of the spine and in 6 out of 18 patients who had had no irradiation previously; thus it was not related to previous radiotherapy. The myeloid : erythroid ratio was normal in both groups; there was therefore no evidence of stimulation of the bone marrow by the dosages of radiation given to the spine.

The increase in cellularity affected all the formed elements of the bone marrow, the myeloid and erythroid series both showing normal maturation. The only abnormalities detected were an increase in the number of plasma cells in 10 patients and an increase in the eosinophil count in 4. This is explained on the basis of a body reaction to foreign protein, associated with an increase in the plasma globulin fraction; the plasma protein values were not studied, however, in the present investigation. *P. I. Reed*

1252. **Ankylosing Sacro-iliitis.** (La sacroileite anchilosante)

A. Robecchi and L. Mussa. *Minerva medica* [*Minerva med. (Torino)*] **1**, 1319–1326, May 2, 1956. 4 figs., 34 refs.

The term ankylosing sacro-iliitis is used by the authors to describe a syndrome which they discuss and differentiate from other types of sacro-iliitis and from spondylitis ankylopoietica. Essentially, there is an ankylosing process involving the sacro-iliac joints and no other. Clinically, the condition is characterized by lumbosacral or sacro-iliac pain on one or both sides, sometimes radiating to the coccyx but without signs or symptoms suggesting involvement of the rest of the spinal column or of rheumatoid arthritis. The radiographic changes in the sacro-iliac joints are those of spondylitis ankylopoietica; the rest of the vertebrae are normal. The natural history of the syndrome is extremely diverse, rendering prognosis difficult. In this paper from the Ospedale Maggiore, Turin, 2 cases are described, in both of which signs localized to the sacro-iliac joints had been present for over 15 years.

[Laboratory findings are not mentioned except that one patient had an erythrocyte sedimentation rate (Westergren) of 20 mm. in the first hour; treatment is not discussed.]

The authors discuss in detail, with many references to the literature, the differentiation from other conditions affecting the sacro-iliac joints, including sacro-iliac osteoarthritis, epiphysitis, osteochondritis, sacro-iliitis of infective, rheumatoid, tuberculous, and senile degenerative origin, and sacro-iliitis condensans. The authors admit that ankylosing sacro-iliitis may be a precursor or a *forme fruste* of spondylitis ankylopoietica and suggest that the diagnosis be kept provisional, bearing in mind the possibility of spread to other spinal segments. *David Friedberg*

1253. **The Course of Rheumatoid Arthritis during Four Years of Induced Hyperadrenalism (IHA)**
D. S. HOWELL and C. RAGAN. *Medicine* [*Medicine (Baltimore)*] **35**, 83–119, May, 1956. 3 figs., bibliography.

The authors, working at the Presbyterian Hospital (Columbia University), New York, have studied the effects of prolonged hormone therapy (" induced hyperadrenalism ") in 68 cases of rheumatoid arthritis (4 initially juvenile) and 7 of ankylosing spondylitis. Most of the cases of rheumatoid arthritis were chronic and had ceased to respond adequately to " conservative " treatment (rest, aspirin, and gold therapy). The disease had been present for over 3 years in 90% of cases, 75% of the patients were female, and 66% were between 40 and 60 years of age. Progress was estimated (1) subjectively, by ascertaining the degree of joint pain, stiffness, tenderness, and functional capacity; (2) objectively, by noting the amount of joint swelling and effusion, deformity, nodules, synovial pouches, and tenosynovitis; (3) by serial recording of erythrocyte sedimentation rate (E.S.R.), pyrexia, haemoglobin value, body weight, differential sheep cell agglutination titres, and the results of streptococcal agglutination tests; and (4) by observing the radiological changes in the joints. The adrenocortical hormones were given for periods ranging from 6 months to 5½ years, 63 of the patients receiving cortisone only, 4 ACTH (corticotrophin) only—7 received both hormones on separate occasions—and one hydrocortisone. The dosage was " as commonly employed elsewhere "; only one patient was given 100 mg. of cortisone daily after the first 2 years, the dosage being smaller in the remainder. In addition, all the patients were given aspirin, 36 to 72 grains (2·4 to 4·8 g.) daily; in 12 cases phenylbutazone was given for 1 to 8 months and in 5 gold therapy for 9 to 18 months in an attempt to reduce the daily dose of hormone required.

The treatment had no apparent effect on the progression of bone and joint damage and of deformity. Disease activity, as estimated by elevation of the E.S.R., persistence of mild anaemia, and positivity of the differential sheep cell and streptococcal agglutination reactions, was similarly unaffected. New nodules appeared in 28 patients. Subjectively, moderate to marked relief of joint symptoms was described by the majority of patients and persisted to the same degree throughout treatment. (The dosage of the hormones was regulated to give suboptimal relief of symptoms in order to eliminate untoward reactions which tended to occur with the higher doses). Functional capacity was correspondingly increased with the relief of symptoms. Phenylbutazone and gold therapy had no appreciable effect in reducing the hormone dosage required. Remissions occurred in 5 cases after 10 to 25 months' treatment, but 3 of these patients relapsed.

The usual side-effects associated with such hormone therapy were observed, that is, psychiatric phenomena, cardiovascular and electrolyte disturbances, peptic ulceration, infections, metabolic and endocrine disorders, and skin and superficial tissue changes. These events tended to occur most frequently in patients with associated disease and debility, and necessitated hormone withdrawal in 37 cases, in 10 temporarily and in 27 permanently.

The authors conclude that there is a place for prolonged hormone therapy in a limited group of selected patients with severe rheumatoid arthritis of long duration which has not responded to rest, aspirin, and gold therapy, provided that these patients are free of any major contraindication to hormone therapy and do not require doses of cortisone exceeding 100 mg. per day. They suggest that borderline cases should receive a preliminary trial course of hormone therapy for 4 or 5 weeks, but that a return to simpler treatment should be made as soon as the patient's condition allows it.

[The simultaneous administration of aspirin, although stated to have little effect, tends to limit the value of these results, which the authors attribute solely to the hormone therapy.] *M. Kendal*

1254. **Comparison of Cortisone and Aspirin in Treatment of Juvenile Rheumatoid Arthritis**
B. M. ANSELL, E. G. L. BYWATERS, and I. C. ISDALE. *British Medical Journal* [*Brit. med. J.*] **1**, 1075–1077, May 12, 1956. 3 figs.

From the Canadian Red Cross Memorial Hospital, Taplow, Bucks, comes this report of the results of a comparative therapeutic trial of cortisone and aspirin in the treatment of juvenile rheumatoid arthritis (Still's disease), which for this purpose was defined as starting before the age of 16. Of the 25 children in the trial, 13 were treated with cortisone and 12 with aspirin, the selection being random and the two groups being almost identical clinically at the beginning of treatment.

The standard dosage of cortisone for the first week was 300 mg. on the first day, 200 mg. on the second, and then 100 mg. per day for 5 days, after which the maintenance dose was determined. At the end of one year the dose of cortisone was between 50 and 100 mg. per day for 6 patients; of the remaining 7, one was now receiving aspirin, having derived no benefit from cortisone, one had been excluded from the trial because of dislocation of the hip after 6 months, and the remaining 5 did not need medication. The dosage of aspirin for older children was 6 g. a day for the first week, 2 g. a day for the second week, and then between 3 and 6 g.

a day. At the end of one year regular aspirin treatment was maintained in only 6 of the original 12 patients, in a dosage of 1·3 to 4 g. a day, the other 6 needing no regular medication. Radiographs were taken of the affected joints in all cases before treatment and at the end of one year.

Assessment of the results showed that these were comparable to those in the similar trials on adult patients carried out under the auspices of the Medical Research Council, except that in the present trial a higher proportion of patients improved than was the case with the adults. In both treatment groups the children improved clinically and functionally to a similar extent. Radiography showed that there was an increase in the number of patients with erosions, this number rising from 3 before treatment to 6 at the end of one year in the cortisone group, and from 2 to 5 in the aspirin group. Side-effects attributable to the drugs were few and in no case were they serious. *Kenneth Stone*

1255. **The Hemagglutination Test for Rheumatoid Arthritis. III. Clinical Evaluation of the Sheep Erythrocyte Agglutination (S.E.A.) Test and the Gamma Globulin (F_{II}) Tests**

A. S. JACOBSON, W. H. KAMMERER, J. WOLF, W. V. EPSTEIN, and G. HELLER. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 490–499, April, 1956. 3 figs., 14 refs.

The authors of this paper from the Veterans Administration Hospital, Bronx, New York, report experience of two serological tests for rheumatoid arthritis which were carried out on 1,576 patients. The sheep erythrocyte agglutination (S.E.A.) test was performed with selected sheep erythrocytes sensitized with a 1-in-20,000 dilution of antiserum (one-tenth of the basic agglutination titre) in 2% sheep serum (complement inactivated). Naturally occurring agglutinins were first absorbed from the test serum. The titration was carried out in saline and in dilutions of sheep serum, the result of the test being considered positive if the titre in sheep serum diluent was 4 or more times greater than that in saline diluent. In the gamma-globulin or Fraction-II (FII) test a suspension of tannic-acid-treated sheep erythrocytes in buffered saline sensitized with pooled human gamma globulin was added to the test serum in saline dilutions. A positive reaction was one in which maximal agglutination was observed at a dilution of 1 in 28 or more.

The results of the first test performed on each patient, which are tabulated, were as follows. In peripheral rheumatoid arthritis 62% of 331 patients gave a positive reaction to the S.E.A. test, whereas 69% of 180 gave a positive reaction to the FII test. When the two tests were carried out simultaneously on serum from 46 patients correlation was good in 39 instances and poor in 7. Of patients suffering from rheumatoid arthritis with spondylitis, 26% gave a positive reaction to the S.E.A. test and 33% to the FII test. A much smaller percentage of patients with rheumatoid spondylitis alone gave positive reactions (2·1 and 3·6% respectively). In patients with psoriasis and arthritis the percentage of positive reactions was 22 to the S.E.A. test and 29 to the FII test. Among patients with other arthritic conditions no group showed any significant incidence of positive results (higher than 10%), although some positive results were obtained in all, particularly in lupus erythematosus. [For results in other types of connective-tissue disease the original must be consulted.] Of 560 patients without any arthritic condition only 3 gave a positive reaction to the S.E.A. test and only 2 to the FII test.

The percentage of initial positive reactions in rheumatoid arthritis increased with the severity of the disease and the degree of incapacity, although 2 patients gave a positive reaction simultaneously with the onset of clinical symptoms. Of patients with nodules, 95% gave positive reactions to the S.E.A. test.

In most instances the results obtained with joint fluid were similar to those obtained with serum. [This paper will repay detailed study.] *L. E. Glynn*

1256. **Agglutination and Inhibition by Serum Globulin in the Sensitized Sheep Cell Agglutination Reaction in Rheumatoid Arthritis**

M. ZIFF, P. BROWN, J. LOSPALLUTO, J. BADIN, and C. MCEWEN. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 500–509, April, 1956. 15 refs.

The introduction of the Waaler–Rose test marked a great advance in the serological diagnosis of rheumatoid arthritis. The original test, in which whole serum was used, was relatively insensitive, detecting only between 40 and 60% of cases. In this paper from the New York University College of Medicine, an investigation is reported which appears to carry this advance much farther. The agglutinating factor in rheumatoid arthritis serum was concentrated in the euglobulin fraction by dialysis against M/150 citrate–phosphate buffer at *p*H 5·8 for 2 days. The euglobulin, dissolved in isotonic saline buffered at *p*H 7, was then used in place of the whole serum in the Waaler–Rose test. With this reagent the results were positive in 76 out of 83 cases, compared with 62 out of 83 when the whole serum from the same patients was used.

Many of the false negative results obtained with whole serum are apparently due to the presence of an inhibitor substance that remains in the supernatant fluid when the euglobulin is precipitated. In non-rheumatoid subjects, however, a considerable proportion of this inhibitor substance is precipitated with the euglobulin. This difference of precipitability in rheumatoid and non-rheumatoid subjects has been developed into a highly selective test for rheumatoid arthritis. Whereas the inhibitor substance was absent from the euglobulin fraction of all the 83 patients with rheumatoid arthritis, it was present in 96% of controls. In a second series of 46 patients and 38 controls the test gave the correct result in every instance.

The results of these tests on patients with Still's disease, spondylitis, and psoriatic arthritis lent support to the view that of these three conditions only Still's disease is to be identified with rheumatoid arthritis.

L. E. Glynn

Neurology and Neurosurgery

1257. **Autonomic Hyperreflexia and its Control in Patients with Spinal Cord Lesions**
N. B. KURNICK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 678–686, April, 1956. 4 figs., 10 refs.

In quadriplegic patients with lesions above the thoracic autonomic outflow, distension of the urinary bladder causes reflex arteriolar spasm which is uninhibited by higher centres. The bradycardia reflexly induced by the carotid and aortic receptors scarcely diminishes the resultant hypertension, and these receptors also affect the vasomotor centres in the medulla, causing vasodilatation and sweating which is restricted to the head and neck.

At the Veterans Administration Hospital, Long Beach, California, the intravenous administration of the two sympatholytic agents phentolamine and 2-(piperidylmethyl)-1:4-benzodioxan failed to control vesical spasms resulting from bladder distension. Hexamethonium chloride, however, in doses of 12·5 to 25 mg. intravenously, was effective in 38 patients with spinal-cord lesions, while oral administration of 250 mg. of hexamethonium, the effect of which lasted up to 4 hours, was of considerable value in bladder training in 30 out of 33 other quadriplegic patients, although in the remaining 3 cases there was a marked aggravation of their pre-existing orthostatic hypotension. Vesical spasms, bradycardia, and piloerection were controlled more easily than the reflexly induced hypertension, probably because only ganglionic transmission is cholinergic in the sympathetic nervous system. The author concludes that the inefficacy of sympatholytic agents suggests that these drugs are more effective in preventing the action of circulating hormones than in blocking sympathetic myoneural transmission. *J. Foley*

1258. **Duration of Vasodilatation after Lumbar Sympathectomy**
A. MCPHERSON and A. W. L. KESSEL. *Lancet* [*Lancet*] **1**, 713–715, May 19, 1956. 2 figs., 34 refs.

The blood flow in the feet of patients who had undergone lumbar sympathectomy for the relief of vascular symptoms after poliomyelitis was measured, the object being to determine the duration of vasodilatation after this operation. For purposes of control the blood flow in the feet of patients who had had poliomyelitis but had not been subjected to sympathectomy and that of healthy subjects were also estimated. Blood flow was determined by venous-occlusion plethysmography after the legs had been warmed: (1) with the patient at rest covered by a blanket; (2) after heating the trunk and arms to induce reflex vasodilatation; and (3) after application of ice to the forehead to induce reflex vasoconstriction.

The values obtained in patients who had not been operated on were very similar to those in healthy subjects. The technical quality of lumbar sympathectomy (18 operations on 14 patients) was assessed from the operation records; in 9 instances it was considered to be good, in 8 it was bad, and in one it was doubtful. The foot blood flow was measured one to 15 years after operation. After a good operation, in which, as a rule, all the lumbar ganglia were removed, a considerable increase in foot blood flow persisted up to 15 years, the mean resting value in such cases being 13·2 ml. blood per 100 c.cm. of tissue per minute, compared with a mean control value of about 3 ml. Vasomotor reflexes could not be induced in these feet. After a bad operation such reflexes were present, and the mean resting foot flow was only 4·5 ml.; nevertheless, several of these patients had had good symptomatic responses for as long as 2 years. *C. J. Longland*

BRAIN AND MENINGES

1259. **Results of Bilateral Intermediate Midbrain Crusotomy in Seven Cases of Severe Athetotic and Dystonic Quadriparesis**
R. MEYERS. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **35**, 84–105, April, 1956. 3 figs., bibliography.

The early results of surgery in 7 cases of severe hyperkinetic cerebral palsy are described and discussed in this paper from the State University of Iowa. A two-stage bilateral section of the intermediate three-fifths of the crus cerebri was performed—a procedure for which the term "intermediate crusotomy" is proposed. All patients had quadriparesis with tension athetosis, severe dysarthria, and resultant psychological difficulties, and were considered to be beyond education and rehabilitation. In 1949 Walker reported amelioration of a case of hemiballismus after section of the lateral two-thirds of the midbrain crus. The present author considered that section of the intermediate portion of the crus (including the pyramidal tract) bilaterally might be a justifiable empirical procedure in these completely disabled patients, in the hope of relieving dystonia and athetosis. The operative approach was under the temporal lobe of the brain, exposing the brainstem at the free edge of the tentorium. The intermediate three-fifths of the crus was then cut (the length of the incision was usually close to 10 mm.) to a depth of 7 mm. Operation on the opposite side was performed from 2½ to 6 months after the first.

Evaluating the results in terms of reduction in the abnormal movements, relief of contractures, and more ready management of the patient, the author found that there was some benefit in all 7 cases, there being marked improvement in 5, moderate improvement in one, and slight improvement in one. One of the markedly im-

proved patients died on the second day after the second operation. In 2 patients progress was such that they were able to start occupational and speech therapy but, as the author points out, the extent to which there will be neurological, psychological, and social recovery in these patients is a matter for the future [and one on which the justification of this operation will depend]. *J. V. Crawford*

1260. **Motor-cyclists, Crash Helmets, and Head Injuries**
W. LEWIN and W. F. C. KENNEDY. *British Medical Journal* [*Brit. med. J.*] **1**, 1253–1259, June 2, 1956. 7 figs., 7 refs.

The authors point out that there were over one million motor cycles on the roads of Great Britain in 1954 and that in that year 1,148 motor-cyclists, including 181 pillion passengers, were killed as a result of road accidents. Of all fatal road accidents 70% are associated with head injury, and the incidence of this injury is high in motor-cyclists—reaching 92% in some estimates. It thus seems clear that motor-cyclists are more liable to head injury than are other road users and that they run greater risks of severe and fatal injury. While it is difficult to produce definitive figures to show that the wearing of a crash helmet protects the motor-cyclist, evidence is accumulating on this point. Cairns, who recommended the compulsory wearing of such helmets by Army motor-cyclists, considered that they reduced the incidence of fatal head injury. At the present time helmets are worn by not more than one in three civilian motor-cyclists. A difficulty at once appears in assessing the value of the helmet in this group, in that if the protection prevents cerebral concussion the patient will not be included in head-injury statistics and may never attend hospital if he has sustained no other injury. Further, if the rider sustains an immediately fatal injury he will not be brought to hospital either and so will also be lost to a statistical survey. However, in spite of these deficiencies evidence of significance is becoming available. Thus the authors show that of 27 motor-cyclists sustaining fatal head injuries in the period 1949–52 none had worn a crash helmet, none of the 11 in 1953 had worn a helmet, while in 1954–5 only 5 out of 12 with fatal head injuries had worn a helmet. Of these last 5 patients all had multiple injuries, 2 died from extracranial causes, and a third was wearing an unsatisfactory helmet; thus in only 2 of the 12 cases had the helmet failed to protect the head adequately. In contrast, among 14 deaths from all causes in motor-cyclists not wearing crash helmets in 1954–5, all but 2 were from head injury and in 9 cases this was the sole injury. These figures suggest that the wearing of an efficient crash helmet reduces the likelihood of fatal injury from a blow on the head of ordinary severity.

In riders wearing a crash helmet (excluding those not coming to hospital) the incidence of fracture of the skull is the same as in those not wearing a helmet, but the type of fracture is less serious in the former group; thus of 22 patients wearing a helmet at the time of injury, only one sustained a depressed or compound fracture and the helmet in this case was of poor quality, whereas of 117 patients not wearing helmets, 2 sustained closed depressed fractures and 11 compound fractures, in 2 cases with depression. From the point of view of the brain injury (again excluding cases in which the helmet prevents the occurrence of concussion) the severity of the concussion is the same in those wearing and not wearing crash helmets. However, a number of cases are described in which, judging from the damage to the helmet and the severity of the associated injuries, it appeared likely that severe and fatal brain damage would have occurred had a helmet not been worn. It also appears that the helmet not only protects scalp and skull, but also prevents surface bruising of the brain, even in very severe injuries—in which, however, the violent deceleration of the head may produce irremediable damage in the brain stem and basal ganglia.

In the authors' opinion the requisites of an efficient crash helmet are that its outer shell should be tough, not easily deformed, and not too brittle, and its surface should be smooth and free from excrescences to permit gliding over the area struck. Light metal or impregnated wood pulp are suitable materials, and the addition of a peak may be valuable in protecting the eyes and upper face, provided it is flexible and firmly attached. The inner padding of the helmet should absorb a maximum of force and reduce to a minimum the force applied to the head itself; sponge rubber and cork are perhaps the most efficient materials. Protection of the temples is important, whereas reinforcement of the crown is not required.

[This paper produces good evidence of the value of crash helmets in reducing the severity of head injuries in motor-cyclists and should encourage the wider use of this safeguard. As the authors point out, better training schemes for this group of road users and the limitation of the power of machines for use on the public highways also deserve consideration.] *J. E. A. O'Connell*

1261. **Vascular Diseases of the Nervous System. A Series of 315 Cases**
A. A. GLYNN. *British Medical Journal* [*Brit. med. J.*] **1**, 1216–1219, May 26, 1956. 1 fig., 7 refs.

A review is presented of 315 consecutive cases of cerebral vascular disease admitted to St. Mary Abbots Hospital, London, during the years 1951 to 1954, particular attention being paid to the diagnosis, clinical features, and prognosis. Cerebral thrombosis was diagnosed in 164 cases, cerebral haemorrhage in 73, cerebral embolism in 6, arteriosclerosis in 7, and subarachnoid haemorrhage in 31; in 16 cases it was impossible to determine whether the illness was due to infarction or to haemorrhage, while in another 16 there were manifestations attributed to hypertensive encephalopathy; in 2 cases there was hemiplegia. In all diagnostic groups there was a slight preponderance of females. Of the total number of patients, 30% were under the age of 60. It is pointed out that while subarachnoid haemorrhage occurred at an earlier age than did cerebral haemorrhage and thrombosis, the mean age of the patients with subarachnoid haemorrhage was still quite high—42% of such patients being over 60 and 64% over 50. Sub-

arachnoid haemorrhage was usually explosive in onset, but there was little difference as regards the rapidity with which symptoms developed between cases of thrombosis and those of haemorrhage. However, early loss of consciousness was observed in only 22% and 33% respectively of patients with cerebral thrombosis and subarachnoid haemorrhage, as against 62% of patients with cerebral haemorrhage. Hypertension was also more prominent in the last-named group. The prognosis was poor in patients with cerebral haemorrhage; 71 of the 73 died. Of the 164 patients suffering from cerebral thrombosis, 60 (36·6%) died, and of 31 with subarachnoid haemorrhage, 7 (22·6%) died. Only 11% of the patients who survived an attack of thrombosis recovered completely; 26% were severely disabled; and the remaining 62% made a fair recovery, having some return of function. A comparison of the clinical features and prognosis in cases of cerebral thrombosis and those in hypertensive encephalopathy did not support the view that in the latter type of case mild localized infarcts are produced by thrombi in minor vessels; the clinical picture was different from that seen in cerebral thrombosis and its pathogenesis may be fundamentally different. *John N. Walton*

1262. **An Analysis of the Results of Treatment of Intra-Cranial Vascular Lesions by Carotid Artery Ligation**
R. A. Davis, N. Wetzel, and L. Davis. *Annals of Surgery* [*Ann. Surg.*] **143**, 641–650, May, 1956. 2 figs., 3 refs.

The results of ligation of the carotid artery in the neck in the treatment of a variety of intracranial vascular lesions are discussed in this paper from the Northwestern University Medical School, Chicago. The commonest lesion in the series of 108 patients (aged 9 to 73 years) was intracranial aneurysm, manifested by spontaneous subarachnoid haemorrhage, but vascular malformations and various tumours and fistulae were also seen. Ligation of the common carotid artery in continuity (with braided silk) was carried out in 85 cases, ligation of the internal carotid artery in 6, ligation of both vessels in 15, and ligation with division of the common carotid artery in 2. Of the 75 patients with intracranial aneurysms 48, including 11 who were in various stages of stupor or coma at the time of operation, were alive and economically and socially independent at the time of the report. One patient had a post-operative recurrence of subarachnoid haemorrhage, due, it was thought, to loosening of the ligature. The remaining 27 patients with aneurysms died following ligation, 14 in the immediate postoperative period, 8 from causes not directly attributed to operation, and 5 from progression of the disease after discharge from hospital. All but one of the 14 patients who died in the immediate postoperative period were deeply stuporose or comatose at the time ligation was carried out. Of 19 patients with intracranial arterio-venous fistula subjected to carotid artery ligation, 18 were alive; all except one of these were alert and responsive at the time of operation. There was one death in the group of 7 patients with intracranial angiomatous lesions and 2 deaths in the group of 7 with miscellaneous lesions. The authors consider that to avoid the poor results previously obtained with carotid artery ligation the patient must be in good condition—that is, not suffering from shock and loss of responsiveness—and the operation should be performed under local analgesia. *J. V. Crawford*

1263. **Psychiatric Investigations on Patients with Tumours of the Third Ventricle and Sella Turcica.** (Psychiatrische Untersuchungen an Kranken mit Tumoren des dritten Ventrikels und der Sella turcica)
R. Pia. *Acta neurochirurgica* [*Acta neurochir.* (*Wien*)] **4**, 320–330, 1956. 10 refs.

At the First Surgical Clinic of the University of Vienna the author carried out a psychiatric investigation in 10 cases of tumour of the third ventricle and 8 of tumour of the sella turcica in order to determine whether they presented specific syndromes which could have localizing or diagnostic value. Before treatment in 6 of the 10 patients with third-ventricle tumours a moderately severe amnestic syndrome was present, sometimes with euphoria or depression and *Witzelsucht*. Among the 8 patients with sellar tumours, on the other hand, only one showed psychiatric symptoms (euphoria). After operation and deep *x*-ray therapy, however, all 18 patients showed psychological abnormalities, even though the treatment had relieved a raised intracranial pressure in 10 of them. These changes were organic in type and similar to those found after an injury involving the brain. The patient's personality before operation was found to play a considerable role in determining the final state.

The author concludes that psychopathological findings are of no value for the localization of tumours in the region of the midbrain. He suggests that deep *x*-ray therapy may play a part in producing the mental changes, or that the relief of intracranial pressure may reveal personality changes previously concealed by the physical symptoms and signs. *J. B. Stanton*

1264. **The Diagnostic and Prognostic Significance of the Radiological Appearance of the Occipital Bone in Tumour of the Cerebral Hemispheres.** (Диагностическое и прогностическое значение рентгенологического симптома затылочной кости при опухолях больших полушарий)
I. S. Babchin. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] 3–7, No. 3, May–June, 1956. 5 refs.

The author, writing from the Leningrad Institute of Neurosurgery, discusses the significance of the " occipital *x*-ray sign ", which he originally described in 1941, in the diagnosis of intracerebral tumour. This sign consists in rarefaction and thinning of the posterior part of the foramen magnum and of the internal occipital crest, and is mainly characteristic of infratentorial tumours, although it occurs also fairly frequently in association with supratentorial tumours. It is produced by prolonged pressure exerted upon the occipital bone by the herniated cerebellar tonsils. In about 37% of normal persons the cerebellar tonsils descend below the level of the foramen magnum; thus in such individuals an increase in intracranial tension caused by a tumour on

either side of the tentorium will lead to an accentuation of the already present downward projection of the cerebellar tonsils and the formation of a pressure cone. This is less likely to happen in those in whom the cerebellum is, in normal circumstances, entirely above the level of the foramen magnum.

The presence of "Babchin's sign" is of practical importance, since it indicates an advanced state of raised intracranial pressure calling for urgent decompression. As the operation itself is likely to be followed by a still further transient rise in intracranial pressure, every inclination to close the skull permanently should be resisted by the surgeon, even after successful removal of the tumour. *L. Crome*

1265. **Clinical Trials of Transergan in the Parkinsonian Syndrome.** [In English]
S. ELIASSON and S. TEJNING. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 375–379, June 9, 1956. 6 refs.

Clinical trials of a new antispasmodic, "transergan" (β-diethylaminoethyl phenothiazine-10-carboxylate hydrochloride), in 10 patients with Parkinson's disease who had previously received "artane" or atropine are reported from the University of Lund, Sweden. An attempt was made objectively to register tremor by two methods: (1) the amount of carborundum sand lost from a perforated plastic globe attached to the back of the hand was estimated over a period of 3 hours; and (2) the oscillatory part of an electromagnetic loudspeaker was attached to the wrist, and the frequency of tremor, together with maximum and minimum amplitudes, was filmed on a recording oscillograph. Reduced amplitude of movement was also studied by measuring the length of the steps taken by the patient in walking 300 metres. There was fairly good correlation between the objective and subjective effects. Transergan was effective in reducing subjective symptoms without producing sedation, the optimum dose being 200 to 240 mg. daily. Three post-encephalitic patients found the drug to be more effective than the drugs previously taken, while 5 patients considered that their condition had been aggravated. Side-effects included restlessness, paraesthesiae, and somnolence, which necessitated withdrawal of the drug in 3 cases. No abnormalities were noted in the blood or urine. *I. Ansell*

1266. **Epilepsy of Late Onset in the Light of Modern Diagnostic Procedures**
H. DIMSDALE. *British Medical Journal* [*Brit. med. J.*] 1, 1214–1216, May 26, 1956. 1 fig., 5 refs.

In this paper from the Maida Vale Hospital for Nervous Diseases, London, the author attempts to assess the relative usefulness of the various techniques which are available for the detection of a lesion in cases of epilepsy of late onset, the material consisting of a series of 200 cases with onset after the age of 20, excluding cases of trauma and those with papilloedema. Clinical and plain *x*-ray examinations were carried out in all cases, but in the first 100 cases the routine procedure was pneumoencephalography by the lumbar route, whereas in the second 100 cases electroencephalography (EEG) was performed, with pneumography in 88 of the cases and angiography in 68. There was little difference in diagnoses between the two groups, and the incidence of space-occupying lesions (excluding angiomata) was about the same in the two groups. Cerebral atrophy presenting as epilepsy was seen in just under one-fifth of the total number of cases. Epilepsy was attributed to arteriopathy or arteriosclerosis in 4 cases in the first group of 100 cases and 3 in the second.

It was found that the EEG was of positive value, especially if localizing delta activity was present. Pneumoencephalography was slightly more reliable than angiography in demonstrating the presence of a tumour at an early stage and also cerebral atrophy. The most suitable diagnostic technique was a combination of EEG with pneumoencephalography by the lumbar route. The author recommends angiography in cases with frank lateralizing signs or bruit; this procedure is not considered to be of any special value, however, in cases of atrophy and is associated with certain risks in cases of arteriopathy. *C. Elston*

DEMYELINATING DISEASES

1267. **Statistical Studies of the Problem of Disseminated Sclerosis. IV. The Process of Gestation and Disseminated Sclerosis. V. Results of Treatment.** (Statistische Untersuchungen zum Problem der Multiplen Sklerose. IV. Gestationsprozess und Multiple Sklerose. V. Therapeutische Ergebnisse)
K. KULIG, G. SCHALTENBRAND, and L. ABB. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **174**, 460–468 and 469–481, 1956. 2 figs., bibliography.

These two articles form part of a series in which various aetiological and therapeutic aspects of disseminated sclerosis have been studied by the statistical analysis of 1,420 cases at the University Neurological Clinic, Würzburg [see *Dtsch. Z. Nervenheilk.*, 1956, **174**, 199 and 219; *Abstracts of World Medicine*, 1956, **20**, 144 and 145]. Of 730 female patients questioned, about 7% stated that the symptoms became worse just before or during menstruation. Of 370 patients who were asked about the effects of pregnancy and parturition, 23% had had a miscarriage or stillbirth before or since the onset of the disease, 23% stated that they had first noticed signs of the disease during pregnancy or the puerperium, 15% stated that the symptoms became worse during pregnancy or the puerperium and 3% that they improved, while 35% had passed through one or more pregnancies without noticing any change. The authors consider that if the termination of pregnancy is to have any beneficial effect it should be performed early, preferably within the first 10 weeks. From a detailed analysis of a larger group and comparison with the general population it was concluded that there was no increase in the incidence of abortion, prematurity, or stillbirth amongst the women affected with disseminated sclerosis.

In the second article the various forms of treatment undergone by these 1,420 patients are detailed. These

included, in the order of frequency with which they produced subjective improvement, mercury inunctions, a diet of uncooked vegetables, arsenic, blood transfusion, physiotherapy, radiotherapy, vitamins, penicillin, quinine, and removal of focal sepsis. These were also tried in various combinations and, although the great difficulty of assessing their value is pointed out, the greatest degree of improvement, both subjective and objective, appeared to result from a combination of mercury inunction, bed rest, vitamins, blood transfusions, radiotherapy, and vegetarian diet, 14 (41·2%) of 34 patients who underwent this treatment showing objective improvement and 20 (58·8%) reporting subjective improvement. The most marked improvement in the cerebrospinal fluid was obtained with arsenic, radiotherapy, and mercury.

[It does not appear from the figures given that any particular line of treatment was more beneficial than the others. There is an extensive bibliography.]

G. S. Crockett

1268. **Multiple Sclerosis in Children**
N. L. Low and S. Carter. *Pediatrics* [*Pediatrics*] **18**, 24–30, July, 1956. 31 refs.

NEUROMUSCULAR DISEASES

1269. **Heredofamilial Juvenile Muscular Atrophy Simulating Muscular Dystrophy**
E. Kugelberg and L. Welander. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 500–509, May, 1956. 2 figs., 26 refs.

The authors describe, from the Serafimer Hospital, Stockholm, and Sahlgrenska Sjukhuset, Gothenburg, 12 cases of juvenile muscular atrophy occurring in patients belonging to six families. The condition was characterized by progressive weakness and wasting first of the muscles of the pelvic girdle and thighs and then later affecting those of the shoulder girdle and upper arms. The age at onset varied from 2 to 17 years, with a mean of 9·7 years. There was no sensory impairment; fasciculations in the limb muscles were observed throughout the disease. The condition appears to run a very slowly progressive course; 2 of the patients became unable to walk at the age of 8 or 9 years, but 7 could still walk 20 years and one 40 years after the onset. In all cases the muscles of the hands remained unaffected.

In each case the condition had originally been diagnosed as muscular dystrophy, but electromyography carried out by the authors showed changes typical of lower motor neurone disease and muscle biopsy in 5 cases confirmed this. The authors suggest that this is a distinct disease entity with hereditary and familial tendencies which seems to be little known. They believe that the increasing use of electromyography and biopsy may show that cases of this condition are commoner than has been supposed. The differential diagnosis from other types of muscular atrophy, particularly the Werdnig–Hoffmann spinal muscular atrophy of early childhood, is discussed.

[The increasing interest in diseases of muscle may reveal hitherto unrecognized syndromes, of which this may well be one. It will be interesting to learn in due course the necropsy findings in these cases.]

N. S. Alcock

1270. **Fatalities in Myasthenia Gravis. A Review of 39 Cases with 26 Autopsies**
L. P. Rowland, P. F. A. Hoefer, H. Aranow, and H. H. Merritt. *Neurology* [*Neurology*] **6**, 307–326, May, 1956. 4 figs.

Between 1930 and 1955 at the Columbia–Presbyterian Medical Center, New York, myasthenia gravis was diagnosed in 180 cases, 55 (30%) of which were fatal. The records of 39 of these fatal cases have been analysed in order to determine the factors responsible for death. The average duration of symptoms in these patients (13 men and 26 women) was 2·8 years. This figure, it is suggested, may indicate that this group of patients suffered from a more malignant form of the disease than is usually encountered. Death was sudden and unexpected in 13 cases. In several of these there had been acute episodes of dyspnoea, before the final attack, which were relieved by neostigmine. The authors consider that these attacks should be recognized as premonitory, and that the maintenance dose of neostigmine should then be increased. All except 2 of the 16 patients who were in a mechanical respirator at the time of death had been cyanotic, comatose, or apnoeic before this treatment was instituted. Pulmonary lesions were found in all the patients in this group on whom necropsy was performed.

In several patients there was little or no response to large amounts of neostigmine in the terminal phases, and in a discussion of treatment the authors state that refractoriness does not depend on the amount of neostigmine given or the duration of administration. They emphasize that administration of barbiturates, opiates, and placebos to patients with ventilatory insufficiency may be dangerous.

At necropsy a thymoma was found in 6 patients; in addition there were 3 cases in which thymomata had been removed surgically and 3 in which there was radiological evidence of a mediastinal mass thought to be thymoma. Thus thymic tumours were present in at least 12 of the 39 cases. Possibly fatal complicating diseases were present in 10 patients, but muscle weakness played a prominent part in the circumstances preceding death. Death was associated with pregnancy in 2 cases and thyrotoxicosis in 2; the variable influences of these conditions on the course of the myasthenia are discussed. Respiratory infections preceded the terminal crisis in 10 cases; there was no overt precipitating factor in 17 others. Lymphorrhages occurred in the muscles of 15 patients. Nodular myositis was present in 3, extensive myocarditis in 2, and focal myocarditis in one patient. The authors state that the significance of these lesions is uncertain, but their occurrence seemed to be more than coincidental.

[This paper should be read by all who are concerned with the management of myasthenia gravis.]

J. MacD. Holmes

Psychiatry

1271. **Alcoholism in Women.** (Alcoolisme féminin)
—. MASCOT, —. HAMEL, and —. DELIRY. *Journal de médecine de Lyon* [*J. Méd. Lyon*] **37**, 265–269, April 5, 1956.

Alcoholism among women is becoming increasingly common in France. In support of this statement the authors cite the fact that the number of admissions for alcoholism to the St. Madeleine Mental Hospital, a psychiatric hospital serving the mainly rural *départements* of Ain and Saône-et-Loire, rose from 25 in 1953 to 39 in 1955, an increase of 56% in 2 years. Abnormal family relationships were found in a high proportion of these cases. In 37% the father was alcoholic and 53% of the patients had alcoholic husbands. The type of marriage contracted was abnormal in 60%; for example, in 30% the husband was either much younger or much older (from 12 to 20 years) than the wife, and in a further 30% marriage was entered into late in life. However, 10% of the patients were spinsters, and 29% had been employed in cafés or wine-shops. In some cases psychological crises and physical illness appeared to precipitate the alcoholism, but in these there was often also a basic personality disorder.

A Freudian explanation of the need for alcohol is attempted. Alcoholism among women is regarded as a "toxicomania" and as only one manifestation of a disturbed personality. In the authors' view it can to some extent be regarded as the price of the emancipation of women.

L. G. Kiloh

1272. **An Investigation of the Home Circumstances of Schizophrenic Patients.** ("Geordnete Familienverhältnisse" späterer Schizophrener im Lichte einer Nachuntersuchung)
K. ERNST. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **194**, 355–367, 1956.

In an investigation of the case histories of 50 unselected schizophrenic patients being treated at the University Psychiatric Clinic, Zürich, the author found 43 with apparently full details of the home life and family situation in which the patient had grown up. In 8 of the 43 cases, according to the history, the home life seemed ordinary and in no way exceptional, but on closer investigation of these 8 cases, including interviews with as many relatives as possible, he found only one family without emotional difficulties in the home, the conflicts in the families of the other 7 patients being depressing, disturbing, and of a chronic nature. As the author points out, a full and reliable history of this kind can be obtained only by visiting the house of the patient and acquiring the confidence of the family. The concept of the "broken home" is criticized; it may be socially useful, but psychologically it has only limited significance. In the author's words "it is impossible to decide whether it is worse to have a drunkard for a father and a neglected home, or to have an embittered woman for a mother and a clean and orderly home and household." The study of the background of a reputedly "orderly" family life may make it easier to understand the psychotic patient and his psychosis.

[This is a critical paper, which exposes the superficiality and carelessness of certain methods of psychiatric history-taking and the misapplication of widely used terms in psychiatry. The author shows how more exact information can be helpful therapeutically.]

W. Mayer-Gross

1273. **Chlorpromazine (Thorazine) for Mental Illness in the Presence of Pulmonary Tuberculosis**
H. PLEASURE. *Psychiatric Quarterly* [*Psychiat. Quart.*] **30**, 23–30, Jan., 1956 [received June, 1956]. 4 refs.

During a period of observation of 4 months, chlorpromazine did not appear to influence the symptomatology or extent of disease as shown by *x* ray, in 32 patients having active pulmonary tuberculosis and receiving antituberculosis drugs. They were compared with 25 patients receiving placebos. Some incidental observations concerning the effectiveness of chlorpromazine and the side reactions to it are also reported.—[Author's summary.]

1274. **Neurotoxic Reactions Resulting from Chlorpromazine Administration**
R. A. HALL, R. B. JACKSON, and J. M. SWAIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 214–218, May 19, 1956. 14 refs.

At Agnews State Hospital, Agnew, California, neurotoxic reactions were observed in 36 out of 90 chronic, semi-disturbed schizophrenics who had received chlorpromazine for about 2 months. The daily dose of the drug varied from 150 to 600 mg. Symptoms appeared 20 days after treatment started and lasted until 17 days after it ceased. In some cases definite signs of a Parkinsonian condition persisted for more than 60 days after cessation of treatment. Complete absence of arm swing was regarded as a sensitive indicator of a neurotoxic reaction. No association between this reaction and liver dysfunction was observed. There was an increase in the cerebrospinal-fluid pressure in half of the cases, but no other changes in the cerebrospinal fluid were noted.

G. de M. Rudolf

1275. **Deaths following Electrotherapy. Report of Five Deaths, with Autopsy Findings in Four Cases**
S. P. ALEXANDER, L. H. GAHAGAN, and W. H. LEWIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 577–581, June 16, 1956. 17 refs.

Dermatology

1276. **Soap and the Skin. With an Investigation into the Properties of a Neutral Soap**
I. MARTIN-SCOTT and A. G. RAMSAY. *British Medical Journal* [*Brit. med. J.*] **1**, 1525–1528, June 30, 1956. 10 refs.

Most ordinary soaps are alkaline, and although synthetic detergents can be made with a *p*H of 6 to 10, the 7 most popular brands were found to have a *p*H range of 8·3 to 9·7. An investigation is reported of the effect on the skin of a neutral soap, made with triethanolamine instead of sodium or potassium, with a *p*H of 7·5. Washing with ordinary toilet soap raised the fatty-acid content of the skin fat, but after washing with the neutral soap this value was almost unchanged. The *p*H of the skin surface after washing with toilet soap was 8 and fell during the following 25 minutes to 5; when neutral soap was used the *p*H of the skin surface was 5·8 and remained unchanged for half an hour—a result similar to that obtained after washing with alcohol. These results suggest that no layer of neutral soap was adsorbed on the skin surface, as with most other soaps, the neutral soap being easily and quickly rinsed off.

The neutral soap was tried in a number of cases of dermatoses of types which are normally exacerbated by soap; it was tried particularly in patients with very dry skin, eczema, cheiropompholyx, and contact dermatitis. In the vast majority, including a number of cases of infantile eczema, there were no ill-effects. Moreover, patients suffering from subacute eczema who would normally be forbidden to wash with soap were able to use this neutral preparation " with impunity ".

E. Lipman Cohen

1277. **Verrucosis Generalisata.** [In English]
E. H. HERMANS and J. P. NATER. *Acta dermato-venereologica* [*Acta derm.-venereol.* (*Stockh.*)] **36**, 112–121, 1956. 6 figs., 35 refs.

1278. **The Use of the Antistreptolysin Titre in the Search for Focal Aetiological Factors in Certain Dermatoses.** (L'importanza del titolo antistreptolisinico nella ricerca di componenti focali etiogenetiche di alcune dermatosi)
G. FARRIS and S. ZOCCHI. *Minerva dermatologica* [*Minerva derm.* (*Torino*)] **31**, 149–157, May, 1956. 11 refs.

Focal infection has for long been considered to be at least a contributory factor in some skin diseases. The authors, working at the Dermatological Clinic of the University of Genoa, stipulate that in order to confirm this concept the clinical and laboratory findings must show that there is an increased serum antistreptolysin (ASL) titre, and that elimination of the focus of infection is followed by improvement, at least, in the skin condition and lowering of the titre. They have therefore determined the ASL titre before and after treatment in 45 patients with acute exudative dermatitis, 21 with an obviously pyogenic skin condition, 21 with neurodermatitis, lichen planus, or pruritus, 11 with lupus erythematosus, 4 with rosacea, and several other small groups, the total being 120 patients.

In all cases of contact dermatitis the ASL titre was normal. In many cases showing an exudative eczematoid picture an increased ASL titre was demonstrable and could be explained in some by the presence of a dental abscess or diverticulitis of the colon, but in others no apparent cause could be found, possibly because of temporary quiescence of the focal lesion. In cases of pyogenic skin infection the titre was usually low, as it was also in cases of licheniform eruption, except when associated with some focal lesion as above or chronic tonsillitis. The titre was raised in the cases of lupus erythematosus, in all 4 cases of rosacea, and in 4 out of 5 cases of alopecia areata, in which there were demonstrable focal lesions. Several other small groups of cases are also discussed. In one case of chronic giant urticaria with a raised ASL titre the skin condition cleared up after performance of tonsillectomy.

Thus in cases showing an increased ASL titre the search for a septic focus was almost always successful. Treatment of this focus was followed by a permanent change in the titre, but as the authors point out, a purely focal aetiology cannot properly be ascribed to any of the dermatoses discussed, since other internal and external factors play their part. Nevertheless they conclude that determination of the antistreptolysin titre deserves a place among the diagnostic procedures employed by the dermatologist.

F. Hillman

1279. **Observations on Acne, Seborrhoea, and Obesity**
S. BOURNE and A. JACOBS. *British Medical Journal* [*Brit. med. J.*] **1**, 1268–1270, June 2, 1956. 5 figs., 19 refs.

The natural history of acne and its correlation, if any, with seborrhoea, obesity, and colouring, as revealed in a study of an unselected series of 2,720 soldiers aged 15 to 40 years, are discussed in this paper from the Royal Hospital, Wolverhampton. The severity of the condition was graded as follows: Grade 0, no comedones present; Grade 1, comedones only; Grade 2, comedones with a few pustules or papules; and Grade 3, many comedones and pustules. The incidence of acne was highest at 18 years, but even so, 11% of the subjects of this age were free from the condition. In the younger age groups the face was the commonest site; after the age of 19 the incidence of facial acne declined, the trunk then becoming the predominant site. The incidence and severity of the condition were entirely unrelated to the presence or severity of dandruff. There was no significant variation in the incidence of acne between groups with differing colour of hair, although of the 14 blond

men in the series, 13 had some acne. The incidence of dandruff was significantly higher among men with ginger-coloured hair. Over the age of 20 years men with acne tended to weigh more than those without, but there was no correlation between weight and incidence of the condition in the younger age groups. Subjects in the older age group with acne had a modal weight of 10 lb. (4·5 kg.) above the standard for age and height, compared with 2½ lb. (1·14 kg.) below normal for those without acne. *E. H. Johnson*

1280. **Tinea Capitis due to *Trichophyton sulphureum***
J. M. BEARE. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 193–199, June, 1956. 14 refs.

The author, basing his conclusions on the findings in 82 cases of tinea capitis due to *Trichophyton sulphureum* seen in children during the period January, 1949, to December, 1955, at the Royal Belfast Hospital for Sick Children, expresses the opinion that cases of ringworm of the scalp due to this organism are increasing in number, while infection due to *Microsporon audouini* is becoming very rare. It is likely that a number of cases of tinea capitis due to *T. sulphureum* remain undiscovered because of difficulties in diagnosis, and that these missed cases act as carriers. Thus in the present series the inflammatory reaction was slight in 15 cases and completely absent in 44, making diagnosis extremely difficult. However, in 23 cases there was a severe inflammation, with delayed development of a kerion reaction in 3; these 3 cases are described in detail and discussed. In this type of infection the affected hairs do not fluoresce under Wood's light, but merely appear to be duller than normal.

Since the author's treatment of these cases was experimental and constantly changing he comes to no definite conclusions, except that *x*-ray epilation seems to be justified only when large areas are involved. For milder cases treatment with a greasy fungicide is recommended, although it is doubtful whether this type of treatment has any value except in preventing the spread of infection. It is assumed that spontaneous cure occurs within a year; the formation of a kerion shortens this period. The author allows the children to go to school and they need not wear special caps, provided the parents co-operate as far as possible in avoiding transmission of the infection. *A. Fessler*

1281. **Suspender Dermatitis and Nickel Sensitivity**
C. D. CALNAN and G. C. WELLS. *British Medical Journal* [*Brit. med. J.*] **1**, 1265–1268, June 2, 1956. 8 figs., 5 refs.

It is suggested in this paper from St. John's Hospital for Diseases of the Skin, London, that up to 3% of women attending hospital skin departments show an allergy to nickel. The primary site of the dermatitis, where there is direct contact with the metal, is nearly always the stocking suspender. The appearance at the contact site varies from a few papules to a confluent patch of dermatitis, usually with some excoriation. On the ear lobe there is often exudation, suggesting impetigo. In many instances patients do not seek advice until secondary sites are involved. The mechanism of this spread is not understood, but the distribution is typical, the sites in order of frequency being elbow flexures, eyelids, neck, and inner side of the thighs. The secondary eruption is usually symmetrical and may recur at intervals, irrespective of the activity at the primary site. The reaction to patch tests with nickel sulphate or chloride is always positive. In some of these cases there is often an associated eczema, most commonly of the hands.

Treatment, when there is secondary spread, is difficult. All contact with metal must cease—that is, metal fasteners and jewellery must be removed—and simple lotions applied to the skin. Not infrequently, however, the dermatitis is slow to clear and application of tar paste or hydrocortisone or *x*-ray therapy may be needed. This sensitivity to nickel, which is most common in the young adult, lasts throughout life. Sweat and friction play a part in initiating the dermatitis. Investigation has shown an all-nylon suspender, now available, to be entirely satisfactory. *E. H. Johnson*

1282. **The Treatment of Polymorphic Light Eruptions with Chloroquine**
J. V. CHRISTIANSEN and H. BRODTHAGEN. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 204–208, June, 1956. 1 fig., 5 refs.

At the Finsen Institute, Copenhagen, 58 patients subject to polymorphic light eruption were treated with chloroquine during the spring and summer of 1955, treatment being started in February or March and lasting for an average of 15 weeks. In most cases the daily dose ranged from 250 to 500 mg., but in a few cases up to 750 to 1,000 mg. was found to be necessary. The patients were asked not to avoid sunshine and not to use any protection against it, such as sunshades or ointments.

Only a few of the patients did not respond at all to the treatment, but about 75% of them remained completely free from symptoms. The side-effects were mostly mild, and included blurring of vision, dysphagia, and disturbance of accommodation; however, in one case there was transient methaemoglobinaemia and in 2 patients the hair of the scalp became depigmented. All these side-effects disappeared when the daily dose was reduced or when the treatment was suspended for a few days. In 39 cases the minimum erythema dose was determined with a mercury lamp before and after treatment. Except in those patients who had not responded, a considerable increase in the minimum erythema dose was observed at the end of the course. For this reason it is assumed that chloroquine acts not by increasing the tolerance of the skin to light, but rather by restoring to normal its adaptability to ultraviolet radiation.
A. Fessler

1283. **The Topical Use of Amphomycin and Amphomycin–Neomycin Ointments**
G. A. CRONK and D. E. NAUMANN. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **3**, 142–145, July, 1956. 2 refs.

Paediatrics

PREMATURITY AND NEONATAL DISORDERS

1284. **Retrolental Fibroplasia. A Reduction in Incidence following a Decrease in Use of Oxygen Therapy for Premature Infants**

A. H. PARMELEE, I. S. PILGER, and W. O. AUSTIN. *California Medicine* [*Calif. Med.*] **84**, 424–426, June, 1956. 13 refs.

The incidence of retrolental fibroplasia in premature infants at the Harbor General Hospital, Los Angeles, is discussed. During the period January, 1952, to January, 1955, 453 premature infants were born, of whom 358 survived, and of these survivors 14 (3·9%) had retrolental fibroplasia. The incidence varied inversely with the birth weight, being 75% in infants weighing less than 1,000 g., 14·7% among those weighing from 1,000 to 1,500 g., and 6·6% among infants weighing 1,500 to 2,000 g. at birth; no cases occurred in the group of infants whose birth weight was 2,000 to 2,500 g. Progressively less oxygen was administered to premature infants during 1953 and the first 6 months of 1954, when it was given only for obvious respiratory distress and for not longer than 2 days at a time. Further, the oxygen concentration in the incubators was measured and not allowed to exceed 40%.

The incidence of retrolental fibroplasia fell progressively with each year. Among infants weighing 1,000 to 1,500 g. at birth the incidence in survivors was 23% in 1952 and 16·6% in 1953; there were no cases in 1954. Among infants weighing 1,500 to 2,000 g. at birth the corresponding figures were 18·1%, 6·2%, and *nil*. Of 55 infants born during this 3-year period and weighing under 1,000 g. at birth, only 4 survived and 3 of these had retrolental fibroplasia. The authors state that from July, 1953, to September, 1954, a " special low electrolyte formula " was given to all infants weighing under 1,800 g. [which would seem to invalidate the conclusion that the fall in the incidence of retrolental fibroplasia was due to the reduction in the concentration of oxygen and in the duration of oxygen therapy]. The authors found that the reduction in oxygen therapy did not adversely affect the progress even of the smallest infants.

H. G. Farquhar

1285. **The Effects of Foetal Anoxia on the Central Nervous System.** (Le retentissement de l'anoxie foetale sur le système nerveux central)

A. MINKOWSKI and S. SAINTE-ANNE-DARGASSIES. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **1**, 531–553, May, 1956. 26 figs., 38 refs.

The relationship between anoxia and damage to the central nervous system in newborn infants has been a subject of much speculation, owing largely to the difficulty of accurate assessment of anoxia. In this study the authors determined the arterial oxygen saturation at birth and later correlated their findings with the clinical state of the central nervous system and with the electroencephalogram (EEG) in 207 cases, in which blood was taken from the umbilical vein at the moment of birth, that is, before the infant breathed. Both the Van Slyke and the Brinkman methods of oxygen estimation were employed.

The calculated oxygen saturation of arterial blood was found to be raised (above 60%) in 98 cases, normal (50 to 59·9%) in 37 cases, and low (below 50%) in 72 cases, the last group including a number of difficult deliveries. Details are given (and illustrated photographically) of the method of clinical assessment of the nervous system in the newborn, and also the authors' criteria for classification into normal, subnormal, and pathological; only 158 of the 207 infants could be so examined neurologically. Of 107 of these infants with high or normal arterial oxygen saturation, 5 were judged to be slighly abnormal and one pathological in each group; but of 51 with low oxygen saturation, 14 were classified as subnormal and 15 as pathological cases. EEG recordings were taken on the first day of life, after the 1st and 3rd weeks, at the 1st, 3rd, 5th, and 8th months, and at one year of age, a total of 450 tracings being obtained. The authors lay special emphasis on postmaturity as an important cause of anoxia and cerebral damage and some evidence is presented in support of the view that in many of these cases labour should be induced. The prognosis was evaluated from an examination of 75 of the infants at 2 years of age, when 6 severely affected cases were found, 3 of which had been classified as subnormal and 3 as pathological at birth.

David Morris

1286. **Plasma Pigments in Erythroblastosis Fetalis. I. Spectrophotometric Absorption Patterns. II. The Level of Heme Pigment; an Early Guide to Management of Erythroblastosis Fetalis**

N. M. ABELSON and T. R. BOGGS. *Pediatrics* [*Pediatrics*] **17**, 452–460 and 461–470, April, 1956. 18 figs., 4 refs.

In the first part of this paper on plasma pigments in erythroblastosis foetalis, which comes from the Children's Hospital and University of Pennsylvania, Philadelphia, the technical methods for spectrophotometric examination of plasma specimens of infants are described, and absorption curves obtained from infants on the first, third, and fifth days of life are reproduced. It was found that the correlation between the presence of abnormal plasma haem pigments and the severity of erythroblastosis was much the same as that between the presence of hyperbilirubinaemia and the incidence of kernicterus. In the authors' view it is possible that both pigments are toxic, and that their effect is additive. It is also possible that the haem pigment owes its toxicity, " if indeed it is toxic ", to the fact that it is a precursor of bilirubin; on the other hand the haem pigment may be innocuous

—" an indicator rather than an aetiological agent of disease ".

In the second part of the paper is reported a study of serial estimations of the plasma haem-pigment level in 135 infants with erythroblastosis foetalis and of the value of this level as an early guide to prognosis and treatment. The need for initial and repeat exchange transfusions was determined by the amount of haem pigment present in the plasma. Failure to control the haem-pigment level was associated with a high incidence of signs of central nervous system involvement and cerebral palsy and with death. The 48 infants in this series whose plasma haem-pigment level was uncontrolled included 15 of the 18 in whom there were abnormal central nervous system signs and 11 of the 13 " failures ". The haem pigments found in erythroblastosis foetalis consist of a mixture of oxyhaemoglobin and a degradation product of haemoglobin. The authors are not prepared to state that the pigments involved play a part in the aetiology of the disease or in the development of kernicterus; they consider that the haem-pigment level is less closely associated with hepatic dysfunction than is the serum bilirubin level. *John Murray*

1287. **Obstructive Jaundice Complicating Hemolytic Disease of the Newborn**

R. Stempfel, B. Broman, F. E. Escardó, and R. Zetterström. *Pediatrics* [*Pediatrics*] **17**, 471–481, April, 1956. 3 figs., 19 refs.

Of 83 erythroblastotic infants seen at Karolinska Sjukhuset, Stockholm, between September, 1954, and June, 1955, 7 had obstructive jaundice. The direct and total serum bilirubin concentrations were estimated by the Ducci–Watson modification of the Malloy–Evelyn method, and serum was examined electrophoretically by the paper-strip technique. In 3 of the infants jaundice was present at birth, and the cord-blood bilirubin levels were respectively 8·63, 10·14, and 12·57 mg. per 100 ml. In all cases hepatomegaly and splenomegaly were noted shortly after birth; an exchange transfusion was given within 3 hours and repeated within 24 hours in all except one case, in which the second transfusion was given on the third day of life. Electrophoretic analysis of the serum failed to reveal any abnormality. The authors discuss the inefficient excretory function of the parenchymal cells of the liver associated with immaturity, and the accumulation of " indirect " bilirubin which results; they also discuss the importance of accumulation of " direct " bile pigment as well as bilirubin itself. When the direct bilirubin concentration is abnormally high at birth exchange therapy may have little effect upon the progress of biliary obstruction. In their view exchange therapy is a much less efficient method of removing bilirubin when erythroblastosis is accompanied by intrahepatic obstruction than when it is not. They doubt whether there is sufficient evidence to justify the use of the serum indirect bilirubin level alone as a guide to treatment.

It is suggested that the direct bilirubin level in cord blood may be of practical importance in the management of haemolytic disease of the newborn. *John Murray*

1288. **The Incidence of Incomplete Descent of the Testicle at Birth**

C. G. Scorer. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 198–202, June, 1956. 3 figs., 4 refs.

In order to determine the incidence of incomplete descent of the testicle 1,700 newborn boys were examined in the maternity department of Hillingdon Hospital, Uxbridge. In babies born at full term the incidence was 3·4%, compared with 30·3% in those born prematurely. In more than 50% of the infants with incomplete descent at birth the testes reached the scrotum during the first month of life. *R. S. Illingworth*

CLINICAL PAEDIATRICS

1289. **Significance of *H. influenzae* in Bronchiectasis of Children**

E. C. Allibone, P. R. Allison, and K. Zinnemann. *British Medical Journal* [*Brit. med. J.*] **1**, 1457–1460, June 23, 1956. 13 refs.

The authors, having previously demonstrated *Haemophilus influenzae* in the sputum of 63 out of 100 adult patients with bronchiectasis, now report an investigation, carried out at the General Infirmary at Leeds, into the occurrence and significance of this organism in the sputum of 32 children aged 4 to 15 years with purulent bronchiectasis. The diagnosis in each case had been established clinically and radiologically. In addition to specimens collected by bronchoscopy under general anaesthesia, antral washings were also examined, and the sensitivity to certain antibiotics and sulphonamides of the organisms isolated was determined.

H. influenzae was present in the bronchoscopic washings in all cases and in antral washings in 19. An attempt was then made to assess the significance of this finding by means of a therapeutic test, for which purpose the authors at first used chloramphenicol. However, it was found necessary to give up to 1 g. 4 times a day by mouth to eliminate the bacteria and reduce the amount of pus expectorated, and in view of reports of blood dyscrasias following high doses of this drug they stopped using it. Neither the tetracycline drugs nor erythromycin given alone was effective, but by combining oxytetracycline or erythromycin with one of the sulphonamides having strong inhibitory action on *H. influenzae in vitro* the good effect of chloramphenicol could be equalled, 2 g. of erythromycin with the same dose of sulphonamide being given daily in most cases.

With this treatment in 27 cases successful clearing of *H. influenzae* and of pus from the sputum occurred in 2 to 12 weeks, after which the treatment was continued on 2 consecutive days each week. Only one case failed to respond. Relapses occurred with an average frequency of once per patient every 6 weeks, and were associated with reappearance of *H. influenzae* in 51% of cases, no bacterial cause being found in 31·9%.

The authors conclude that *H. influenzae* " is responsible for keeping the chronic inflammatory process smouldering in bronchiectatic individuals ".

A. White Franklin

1290. **The Hypothyroid Infant and Child. The Role of Roentgen Evaluation in Therapy**
L. B. Lusted and D. E. Pickering. *Radiology* [*Radiology*] 66, 708–719, May, 1956. 8 figs., 14 refs.

Earlier work at the University of California Medical Center, San Francisco, has shown that the level of dosage of thyroxine required to restore the hypothyroid infant to a superficially normal state of physical development only is below that required to achieve full maturity of bone and normal growth and development of the central nervous system. The evidence suggests that, if given at a sufficiently early stage in the disorder, full and adequate treatment with thyroid extract or sodium L-thyroxine will ensure a skeletal development which corresponds with the chronological age, and that this dosage is similar in amount to that necessary to restore a normal level of function in the central nervous system. Periodic radiological examination and repeated determinations of serum hormonal iodine are the best guides to therapy.

In this paper the histories of 8 cases are given, these being chosen to represent hypothyroid infants in some of whom adequate and in some inadequate therapy had been employed. Serial radiographs of the hand and wrist are shown, starting from the age of a few months when there is much disparity between bone maturity and chronological age. The effect of increase of dosage of thyroxine in cases in which earlier therapy had been inadequate is demonstrated. Mental retardation persisted in those infants in which early diagnosis had not been made, or in which full dosage had been started too late in the course of treatment. In other cases in which full dosage had been instituted early the child was subsequently shown to have normal mental capacity.

A. M. Rackow

1291. **Management of Hypothyroidism in Infancy and Childhood**
R. E. Cooke and E. B. Man. *Pediatrics* [*Pediatrics*] 17, 617–631, May, 1956. 3 figs., 30 refs.

The management of 24 children (including 5 infants under one year) with congenital hypothyroidism is discussed in this paper from Yale University School of Medicine. The diagnosis, suspected clinically, was confirmed by determination of the serum butanol-extractable iodine (B.E.I.) level, which was also used to regulate replacement therapy. The mental development of these patients was relatively poor, although they were receiving treatment generally considered to be adequate. The authors state that if more satisfactory mental development is to be achieved, then earlier diagnosis and more adequate therapy are essential. In their experience the most useful aid in the early detection of congenital hypothyroidism and in determining the adequacy of treatment is the serum B.E.I. level. The young child needs proportionately more thyroid than that indicated by body weight or surface area, but in many instances the recommended method of gradually increasing the dose of thyroid until toxicity is observed is unsatisfactory. The optimum dosage should be based upon the level of circulating thyroxine-like iodine, which should be determined frequently, the serum B.E.I. value being kept between 5 and 7 μg. per 100 ml. after attaining this level as quickly as possible. In conclusion the authors state that to achieve optimum mental development in cretins methods should be developed for the detection of relative hypothyroidism in the foetus and mother before delivery and adequate treatment should probably be started in the prenatal period.

J. M. Smellie

1292. **Idiopathic Hypercalcaemia of Infants**
K. Rhaney and R. G. Mitchell. *Lancet* [*Lancet*] 1, 1028–1033, June 30, 1956. 7 figs., 20 refs.

The clinical and pathological features of 3 fatal cases of the simple form of idiopathic hypercalcaemia are described and compared with those of the severe form and of hypervitaminosis D.

The deaths of these 3 infants have not been satisfactorily explained, but a fatal outcome may possibly have been precipitated by persistent vomiting. Renal calcification was the salient pathological feature in all 3. Most of the deposits of calcium were in the outer medulla, the cortex being only slightly affected. Some of the medullary deposits appeared to be closely related to the loops of Henle and contained amorphous calcium; such deposits were associated with focal degeneration of both interstitial tissue and tubules and with granulomatous inflammation. The rest of the medullary calcium, and the few small cortical deposits, consisted of concretions in the interstitial tissue, and these produced tubular compression and distortion. The renal lesions are not specific, similar changes having been found in cases ascribed to hypervitaminosis D and in infantile renal acidosis, as well as in association with various other diseases of infancy. Metastatic calcification of a cerebral artery and osteosclerosis were present in one of the cases.—[Authors' summary.]

1293. **Idiopathic Hypercalcaemia of Infancy. Clinical and Metabolic Studies with Special Reference to the Aetiological Role of Vitamin D**
J. O. Forfar, C. L. Balf, G. M. Maxwell, and S. L. Tompsett. *Lancet* [*Lancet*] 1, 981–988, June 23, 1956. 6 figs., 45 refs.

The possible relationship between vitamin-D intake and the development of idiopathic hypercalcaemia has been investigated by means of clinical and metabolic studies carried out at the University of Edinburgh between 1951 and 1956 on 6 infants, among whom were a pair of twins, who developed the condition between the ages of 3 and 10 months. All the patients showed the characteristic clinical features, but in one of the twins the blood calcium level was not raised; brief case histories are given. Balance studies were carried out to investigate the effect on calcium and phosphorus metabolism of the addition of vitamin D or cortisone, or both, to the diet. On an unrestricted diet the infants showed an increased retention of calcium and phosphorus, and the addition of calciferol did not cause any greater retention of calcium than would be expected in the normal infant. Serum citrate levels were estimated and found to be low, thus differing from the high levels found in patients with

vitamin-D intoxication. Hypercholesterolaemia was a feature of the cases in which serum cholesterol levels were estimated, and there was a close correlation between the cholesterol and calcium levels in the blood. No abnormal sterols were demonstrated by chromatography.

The authors agree that some of the features of idiopathic hypercalcaemia, for example, the clinical symptoms, the hypercalcaemia, hypercalciuria, and decreased serum alkaline-phosphatase content, could be explained on the basis of vitamin-D intoxication; but point out that other features, such as the absence of clinical change when vitamin D is administered, the increased phosphorus retention, and hypocitraemia, are unlike those of vitamin-D toxicity. It is postulated that the idiopathic hypercalcaemia of infancy results from a disturbance of cholesterol metabolism, with the consequent production of a toxic hypercalcaemic substance. The name "idiopathic hypercholestero-calcaemia" is suggested as a more accurate description of the disease, and this term would embrace those patients who exhibit the typical clinical features but have no hypercalcaemia.

R. M. Todd

1294. **Changes in Total Chloride and Acid–Base Balance in Gastroenteritis following Treatment with Large and Small Loads of Sodium Chloride**
D. B. CHEEK. *Pediatrics* [*Pediatrics*] **17**, 839–848, June, 1956. 3 figs., 25 refs.

Because large amounts of sodium and chloride are frequently given in the initial rehydration of infants with gastro-enteritis the author carried out the following study. Of 17 infants admitted to the Children's Hospital, Cincinnati, with gastro-enteritis, 9 (Group I) received 11 to 25 (average 18) mEq. of sodium chloride per kg. body weight in the first 24 hours, and 8 (Group II) received 6 to 7 mEq. of sodium and 7 to 9 mEq. of chloride per kg. body weight; all were given 3 mEq. of potassium and 200 ml. of water per kg. body weight on the first day. On the following 2 days these quantities were reduced to 150 ml. of fluid, 3 mEq. each of sodium and potassium, and 6 mEq. of chloride per kg. body weight per day. At the time of admission 3 infants in each group were suffering from hypotonic dehydration, one in each group had hypokalaemia, and all showed a moderate to severe acidosis. In all the patients except one in Group II the diarrhoea ceased within 24 hours.

At the end of 24 hours, 5 infants in Group I still had persistent acidosis and 4 hypokalaemia, whereas in Group II only 2 had persistent acidosis and one had hyperkalaemia. At 72 hours, Group-I patients showed a tendency to metabolic alkalosis and 3 had hypokalaemia; excluding one case of recurrent diarrhoea, only one patient out of the remaining 7 in Group II had slight metabolic alkalosis. The author stresses that in infants in whom the diarrhoea persists low sodium loading will of course lead to persistent acidosis and dehydration. Estimations of total body chloride made at the time of admission and at 24 and 72 hours showed chloride deficits in both groups, ranging from 1 to 20 mEq. per kg. body weight on admission, but 6 patients in Group I subsequently showed considerable chloride retention; 2 developed oedema and one of these had convulsions. In 3 patients in Group I, including the 2 with oedema, the ratio of increase in bromide space to increase in total weight suggested the presence of cellular dehydration. In Group II only one patient showed a significant increment in total body chloride. It is considered that in gastro-enteritis the amount of sodium given initially should be similar in magnitude to the known deficit, except in the presence of hyperelectrolytaemia.

K. G. Lowe

1295. **An Unusual Illness in Young Children Associated with an Enteric Virus**
M. CRAWFORD, A. D. MACRAE, and J. N. O'REILLY. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 182–188, June, 1956. 5 refs.

An outbreak of mild illness in 10 babies admitted to the Queen Elizabeth Hospital for Children, London, is described. The principal features were irritability, fever, rash, enlarged superficial lymph nodes, reddening of the fauces and tonsils, vomiting, diarrhoea, and changes in the cerebrospinal fluid. Five strains of virus were isolated in tissue culture. These were found to be immunologically closely related to each other, but distinct from a number of other viruses. Their role in the aetiology of this illness is discussed.—[Authors' summary.]

1296. **Idiopathic Renal Acidosis in Infancy (Lightwood's Syndrome).** (L'acidose rénale idiopathique du nourrisson (syndrome de Lightwood))
M. JEUNE and A. CHARRAT. *Pédiatrie* [*Pédiatrie*] **11**, 205–226, 1956. Bibliography.

A detailed study of idiopathic renal acidosis is presented, based on the findings in 8 cases seen during a period of 9 years at the Hôpital Debrousse, Lyons. The condition occurs in bottle-fed infants of about 4 to 6 months. A distaste for both liquid and solid food develops, followed by vomiting attacks, constipation, failure to gain weight, marked dehydration out of proportion to the vomiting, and muscular hypotonia. On clinical examination the baby appears ill, fretful, marasmic, and dehydrated. Hard faecal masses may be felt in the abdomen, drawing attention to the unusual combination of dehydration with constipation. Striking and unpredictable fluctuations in weight may occur. Except in untreated, severely dehydrated infants the urine is consistently alkaline and frequently contains no abnormal constituents, but biochemical examination of the blood reveals a chronic and persistent acidosis, with hyperchloraemia and a high blood urea level. In untreated cases of long standing radiological evidence of calcification of the renal medulla may be obtained, but its absence does not invalidate the diagnosis. The authors recommend that in all cases chromatographic examination of the urine for amino-acids be carried out to exclude cystine storage disease, which is one of the conditions to be considered in the differential diagnosis. Mild cases with spontaneous recovery do occur, but in the majority of unrecognized and untreated cases the infant dies as the result of a severe metabolic crisis.

Treatment, the results of which are excellent, should be directed towards preventing (1) the occurrence of metabolic crises, and (2) renal calcification by the administration of alkalis over a long period. Sodium citrate in doses of 100 g. daily and citric acid, 60 g. daily, are given to begin with. These doses are steadily increased until a satisfactory clinical, rather than biochemical, result is achieved. This may be measured by the disappearance of anorexia and constipation, and by a gain in weight. Caution must be exercised to avoid overdosage and consequent alkalosis, which is manifested by apathy, anorexia, and diarrhoea, and in extreme cases has a fatal outcome. Treatment should continue until growth has become normal and, ideally, until the blood bicarbonate level has remained normal for several months. The *p*H of the urine always falls below 6 some days after cessation of treatment.

The authors point out that the symptomatology is dependent on the acidosis and the cellular dehydration which it entails. The fundamental metabolic failure is an incapacity of the kidney to excrete an acid urine and thereby to maintain the acid–base equilibrium of the organism. They suggest the following sequence of events. (1) There is a primary failure of the proximal tubules to reabsorb bicarbonate, whence the acidosis. (2) A compensatory excessive reabsorption of chlorine by the proximal tubules occurs, giving rise to hyperchloraemia. (3) The arrival of abnormal quantities of bicarbonate in the distal tubules hinders the formation of ammonia and the excretion of free acids. (4) Calcium ions are mobilized to neutralize the excess of acid ions, and because calcium precipitates easily in an alkaline medium, calcification occurs in the collecting and distal tubules. The tubular dysfunction is considered to be due to functional immaturity, glomerular function being established before that of the tubules. Disharmony in the maturation of the diverse functions of the nephron would explain the age at which symptoms of renal acidosis occur, their transitory character, and their disappearance after some months. *E. S. Wyder*

1297. **The Treatment of Wilms' Tumor**

E. NG and B. V. A. LOW-BEER. *Journal of Pediatrics* [*J. Pediat.*] **48**, 763–769, June, 1956. 17 refs.

Embryoma of the kidney (Wilms's tumour), although infrequent, is the commonest malignant abdominal lesion of infancy. In this paper from the University of California Hospital, San Francisco, 9 cases are reported, 5 in boys and 4 in girls, 6 of the patients being under 3 years of age. The symptoms, which did not occur until an abdominal tumour was palpable, were discomfort, fever, loss of weight, and microscopic haematuria in one case; in no case was gross haematuria seen. The study of pyelograms is essential in order to exclude possible involvement of the opposite kidney. Calcification may be present on the affected side; its presence is said to indicate a favourable prognosis and its pattern to distinguish it from nephroblastoma. Radiographs of the lungs and bones may reveal metastases.

Of the 9 patients, 4 received preoperative as well as postoperative *x*-ray therapy combined with transperitoneal nephrectomy; this route has the advantage of facilitating early ligation of the renal vessels and removal of the tumour, even if massive. In radiotherapy 2,500 r was given over 4 weeks (200 kV with 0·9 mm. Cu and 50 cm. T.S.D.), using anterior, posterior, and occasionally lateral fields, care being taken to avoid irradiation of the opposite kidney. Anorexia, vomiting, anaemia, skin reactions, and the presence of thoraco-lumbar scoliosis made in-patient treatment essential. Of the remaining 5 patients, 3 had advanced disease when first seen and were not considered suitable for the above treatment, while 2 others were treated by nephrectomy and postoperative radiotherapy only. Of the 4 who received the full treatment, one died after 14 months from pulmonary metastases, but the other 3 are alive after 2, 5½, and 6 years respectively. Only one of the patients who received postoperative radiotherapy is alive 3 years after nephrectomy; the other died from involvement of the opposite kidney.

Considering these results together with all cases of Wilms's tumour seen at the hospital since 1926 (a total of 27 with 14 survivors) the authors found that 7 out of 8 treated by nephrectomy plus pre- and post-operative radiotherapy had survived, some for 10 years. Of the patients treated by nephrectomy alone 3 out of 4 survived, and of those treated by nephrectomy and only postoperative radiotherapy 4 out of 7 survived. The authors conclude that the addition of preoperative radiotherapy not only reduces the size of the tumour and facilitates nephrectomy, but also appears to improve the survival rate, and that a further trial of this triple procedure in unselected cases is warranted.

Charles Nicholas

1298. **Evaluation of a Conditioning Device in the Treatment of Nocturnal Enuresis**

F. C. BEHRLE, M. T. ELKIN, and P. C. LAYBOURNE. *Pediatrics* [*Pediatrics*] **17**, 849–856, June, 1956. 1 fig., 5 refs.

The psychological as well as the therapeutic effects of a conditioning device in the management of enuresis were studied at the University of Kansas School of Medicine, Kansas City, in 20 children aged 6 to 14 years. The device was similar to that described by Seiger (*J. Pediat.*, 1952, **40**, 738; *Abstracts of World Medicine*, 1952, **12**, 469), and consisted of a pad which, when wetted with urine, initiated the ringing of a bell. The children were of average intelligence but all except one had been persistent bed-wetters since birth. It was found that in 18 of the 20 children there was at least one other recognized abnormal behaviour trait, such as nail-biting, thumb-sucking, shyness, or a stammer. Emotional disturbances, as reflected by the results of psychological tests, were observed in all the 18 patients with some behaviour trait, while in 7 there was a definite neurotic pattern.

All the children showed some resistance to the treatment, 15 of them endeavouring at times to interfere with the apparatus. Fear reactions were observed in 13. The apparatus was removed from the bed after 7 consecutive dry nights and from the house after 14. In all

except one of the patients there was a beneficial effect; 6 maintained a completely dry bed for periods of 18 to 39 months, and 9 were materially improved, in that they only occasionally wetted the bed; the remaining 4, after responding favourably for short periods, reverted to previous bed-wetting habits. In none of the children did any new symptoms replace the enuresis; indeed, in some there was a general improvement in social behaviour.

The results suggest that this device has a beneficial effect, but, as the authors emphasize, the child's co-operation is essential to a successful result.

E. H. Johnson

1299. **A Trial of Cortisone and ACTH in Infective (Non-specific) Polyarthritis of Children.** (Опыт применения кортизона и адренокортикотропного гормона у детей с инфекционным (неспецифическим) полиартритом) A. B. Volovik. *Педиатрия* [*Pediatrija*] 10–12, No. 2, March–April, 1956.

The author reports the results of the treatment with cortisone or ACTH (corticotrophin) of 13 children, all of whom were suffering from non-specific infective polyarthritis, which in 2 cases had been present for at least 1½ years. Previous treatment with prolonged courses of salicylates, antibiotics, and amidopyrine in conjunction with physiotherapy and orthopaedic measures had had little effect. Cortisone was given in doses of 100 mg. daily (in a few cases 150 to 200 mg.), this dose being lowered by 25 to 50 mg. if oedema or a rise in blood pressure developed. The dose of ACTH was 30 to 40 units daily, gradually decreasing to 7 units daily. Usually only one course of treatment lasting 14 to 38 days was given. A detailed description of 5 out of the 13 cases is presented to illustrate the effect of the hormones.

The results are held to justify the use of ACTH and cortisone in that all the children showed a rapid and often striking improvement in their general state, the temperature falling quickly to normal, with disappearance of pain and joint swellings and lessening of contractures. The increased erythrocyte sedimentation rate returned to normal in nearly all the cases observed.

Edward D. Fox

1300. **Mongolism (Mongoloid Deficiency) during Early Infancy—Some Newly Recognized Diagnostic Changes in the Pelvic Bones**
J. Caffey and S. Ross. *Pediatrics* [*Pediatrics*] 17, 642–651, May, 1956. 6 figs., 10 refs.

The literature contains numerous observations on skeletal abnormalities in mongolism, but very few of these have been made during the first weeks of life, when clinical diagnosis is most uncertain and most important. At the College of Physicians and Surgeons, Columbia University, New York, the authors have studied this problem by examining radiographs of the pelvis of 1,500 unselected newborn infants, including 5 mongols, and of 13 other infants with mongolism. Two angles were measured in each case—the acetabular, by the method of Hilgenreiner, and a new one which the authors term the iliac angle. The first is the angle between the acetabular roof and the horizontal plane, while the second is the angle between the outer border of the ilium below the antero-superior spine and the horizontal.

The mean acetabular angle in normal male infants was 26 degrees, and in female infants 29 degrees, with standard deviations of 4·6 and 4·9 respectively. In mongols the mean figures were 12 degrees in males and 18 degrees in females, the standard deviations being 3·5 and 5·5 respectively. The iliac angle was more constant, the mean for normal infants of both sexes being 55 degrees at birth (S.D. 5·5). The mongols had a mean iliac angle of 45 degrees for both sexes (S.D. 8). The iliac index is derived by adding together both the acetabular angles and both the iliac angles and dividing this by two. The mean value of this index at birth was 81 in normal infants and 62 in those with mongolism.

The authors consider that this index may prove more useful in the diagnosis of mongolism than either of these angles alone. It should be pointed out that obvious mongolism may be present without any skeletal abnormalities; in one of the mongol cases in the present series the angles and the iliac index were well within the normal range.

D. E. Fletcher

1301. **Developmental Aphasia Observed in a Department of Child Psychiatry**
T. T. S. Ingram and J. F. Reid. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] 31, 161–172, June, 1956. 28 refs.

Among 804 patients referred to the Department of Psychological Medicine at the Royal Hospital for Sick Children, Edinburgh, during a period of 18 months there were 78 children of average intelligence who were suffering from developmental aphasia. None of them showed evidence of neural, auditory, or cerebral abnormality to which the symptoms could be attributed. There were 65 boys and 13 girls, their ages varying from 6 to 15 years. A high proportion came from Social Classes I and II, 22% came from broken homes, and there was a high incidence of psychological disturbance in the homes of the others. Tests of laterality showed that 14 (18%) were ambidextrous, while 42 others showed only slight preference; 41 (52%) were left-eyed and 17 (21%) left-footed. Most of the children had shown anxiety symptoms shortly after starting school.

The various types of speech disorder present were studied with the help of tape recordings taken during the psychiatric interview. Dysarthria was found in only 5 cases, whereas articulatory apraxia occurred in 40. The majority of the children had specific difficulties in comprehending speech and in finding words with which to express themselves (receptive and expressive aphasia).

Associated reading and writing disorders (dyslexia and dysgraphia) were common. Treatment was aimed at diminishing anxiety, restoring confidence, and enabling the child to appreciate the shapes and forms of words with his proprioceptive sense. The role of psychological disturbances in the home, crossed laterality, and other factors in the genesis of speech and reading disorders is discussed.

R. S. Illingworth

Medical Genetics

1302. **Familial Tuberous Sclerosis**
W. M. JORDAN. *British Medical Journal* [*Brit. med. J.*] **2**, 132–135, July 21, 1956. 1 fig., 6 refs.

Tuberous sclerosis is a rare disorder of tissue growth, in which many different tissues may be involved. It is hereditary and may be familial: an Anglo-Maltese family is here described in which 4 members were affected. The classic descriptions of the disease, to which the name epiloia was given, concentrated on the symptom triad of infantile epilepsy, mental deficiency, and adenoma sebaceum of the face, and emphasized the bad prognosis. But only about half the sufferers exhibit the disease in this fully developed form, and milder forms with good prognosis occur just as often as the severe ones. The disease is very pleomorphic, and other common manifestations are renal or retinal tumours, and cystic lungs and phalanges. The disease is probably transmitted by an incompletely dominant gene, and in any affected family the pattern of the disease remains constant. Whenever tuberous sclerosis is suspected or diagnosed in a patient the remaining members of the family should be studied.—[Author's summary.]

1303. **A Further Study on the Familial Aspects of Carcinoma of the Stomach**
C. M. WOOLF. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] **8**, 102–109, June, 1956. 17 refs.

In this study, reported from the University of Utah, the author sought to avoid the difficulties (which are discussed) of the usual method of ascertaining the incidence of cancer among the relatives of propositi and control subjects by interview and inquiry. Instead, propositi were selected by noting the names of those dying of cancer of the stomach between 1930 and 1949 in the State of Utah as shown on the State death certificates. In about one-quarter of these cases the name of the father was found in the family group records (totalling some 3,000,000) of the Mormon Genealogical Society archives in Salt Lake City. From these records were obtained the names of the sibs of the propositus, for which a search was then made among the death certificates (available since 1905). In this way histories were collected of 300 families. Controls were selected by noting the name of the next person in the file of similar age and sex and dying in the same county and the same year as each propositus, their family histories being then obtained in the same way.

Of the 991 parents and sibs of the propositi, 66 died from cancer of the stomach and 94 from cancer at other sites (total 160), while among the corresponding relatives of the controls there were 32 deaths from cancer of the stomach and 82 from cancer at other sites (total 114). The difference between the two groups for total deaths from cancer is significant ($P<0.01$), and the difference for deaths from cancer of the stomach is highly significant ($P<0.001$). In regard to other sites the only apparent difference was for cancer of the small intestine. The similarity of these results to those of previous studies is discussed. The author concludes that "heredity plays a role in the occurrence of stomach cancer".
G. C. R. Morris

1304. **Hereditary Factors in the Collagen Diseases. I. Research on Hereditary Factors in Acute Rheumatism.** (Sulla eredopatologia delle mesenchimopatie reattive (cosidette malattie del collageno). I. Ricerche sui fattori ereditari del reumatismo acuto primario)
G. G. NERI SERNERI and V. BARTOLI. *Acta geneticae medicae et gemellologiae* [*Acta Genet. med. (Roma)*] **5**, 155–189, May, 1956. Bibliography.

In this study of hereditary factors in acute rheumatism the index cases were 287 patients (137 male and 150 female) from a total of 368 with rheumatic fever who (when children) had attended the Institute of Pathological Medicine, Florence, between 1940 and 1955. The families of these patients were visited and examined for signs of acute rheumatism—that is, a past history of long-lasting fever with diffuse arthritis, or of chorea even without any joint involvement, or valvular heart disease of rheumatic origin. The families of 300 children attending the clinic for other illnesses were visited and examined in the same way and served as a control group.

The rates of incidence in the two groups were as follows (those for the rheumatic families being given first): fathers 15·6% and 2·6%; mothers 21·9% and 3·0%; brothers 11·4% and 1·6%; sisters 14·7% and 2·1%; sons 8·1% and 1·6%; and daughters 11·3% and 2·4%. In 4 instances both parents of an index patient had had rheumatic fever, and in these families 5 out of 8 children, that is, the index cases, and one of their 4 sibs were affected.

The authors note that no single genetic hypothesis would fit their findings; their preference is for a dominant gene with reduced penetrance. None of the following disorders showed an increased incidence among the relatives of the rheumatic index cases: asthma, urticaria, vasomotor rhinitis, Quincke's oedema, and degenerative connective-tissue disorders. *C. O. Carter*

1305. **The Genetics of Human Haemoglobin Differences: Problems and Perspectives**
J. V. NEEL. *Annals of Human Genetics* [*Ann. hum. Genet.*] **21**, 1–30, July, 1956. Bibliography.

1306. **Infantile Genetic Agranulocytosis (Agranulocytosis Infantilis Hereditaria). A New Recessive Lethal Disease in Man.** [In English]
R. KOSTMANN. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **45**, 309–310, May, 1956.

Public Health

1307. **The Prevention of Burning Accidents. A Survey of the Present Position**

L. COLEBROOK, V. COLEBROOK, J. P. BULL, and D. M. JACKSON. *British Medical Journal* [*Brit. med. J.*] 1, 1379–1386, June 16, 1956. 5 figs., 9 refs.

The authors examine the results of recommendations made by Colebrook and Colebrook (*Lancet*, 1951, **2**, 579) for the prevention of burning accidents in the home, which were based on the findings in 2,000 such cases admitted to the Birmingham Accident Hospital. They review the national mortality figures for burning accidents, report on 1,639 further cases treated at the same hospital since 1951, and discuss preventive measures.

The Heating Appliances (Fireguards) Act of 1952 took effect on October 1, 1954. At the same time attachable fireguards were made available for gas and electric fires already in use, but it is estimated that only about 1·5% of these fires have been so fitted. For guarding the open coal fire, which is still a major hazard, a type of guard which can be hooked on to an ordinary chimney breast is now available, and some local authorities hire fireguards to ratepayers at a nominal annual rent—a service to be encouraged. The increasing awareness of the danger from inflammable clothing materials, whether intrinsically so (such as flannelette and similar fabrics) or rendered so by finishing processes, has led to the manufacture of safer materials and the development of non-inflammable processing. The assessment of inflammability of fabrics by the Standard Flammability Test of the British Standards Institution is described. Some safeguards against scalding are also described; these include a teapot with a wide base and a lid with double lugs, and a table clamp with clips to hold vessels such as jugs containing hot liquid. No great benefit from these improvements is yet apparent, for the annual number of deaths from burns and scalds shows only a small decline—from 946 in 1946 to 781 in 1954.

Of the 1,639 more recent cases of burning or scalding now reviewed, 1,197 occurred in and about the home; among 701 cases of burns there were 94 deaths, and of 496 scalds, 11 were fatal. Half the burns were due to contact with open fires or other heating appliances, the majority of which were unguarded, and about 4 out of every 5 deaths (82%) were due to ignition of clothing, the incidence of this last type of accident having increased from 35% in 1945–50 to 50% in 1951–5. Nightdresses and dresses carried a high risk; thus, 84 children in nightdresses were burnt (resulting in 14 deaths) as compared with only 6 in pyjamas (with one death). Of the 496 cases of scalding (339 in children under the age of 4), this was caused by the overturning of a teapot (95 cases) or other container of hot liquid (172 cases), or by falling into a container, such as a bath of hot water, left on the floor (73 cases).

The authors stress the need to publicize by all possible means the risks still present and the safeguards available. They recommend the display of fireguards at all showrooms of the nationalized gas and electricity services, and urge that local authorities should carry out the recommendations of the Ministry of Housing for the fixing of fireguards and that the Government should encourage, and if need be subsidize, the use of non-inflammable materials for the clothing of children and the elderly.

V. Reade

1308. **A Survey of Domestic Burns and Scalds in Wales during 1955. Some Observations on Their Prevention and the Social Responsibility of the Medical Profession**

M. N. TEMPEST. *British Medical Journal* [*Brit. med. J.*] 1, 1387–1392, June 16, 1956. 3 figs., 6 refs.

The author has investigated 226 cases of burns and scalds occurring in the home and treated at St. Lawrence Hospital, Chepstow, Monmouthshire, during 1955, with special reference to the cause of the accident, the part played by clothing, the social background, and the awareness of parents of hazards in the home and of legislation in respect of fireguards. There were 118 cases of burns, resulting in 24 deaths, and 108 of scalding, with one death. Of the burns, 50 were caused by an unguarded coal fire, 15 by electric fires (2 unguarded), and 4 by gas fires (all unguarded), while 12 were associated with an epileptic fit and 12 with cardiovascular accidents (resulting in 10 deaths). In 74 cases the patient's clothing had caught alight, this being the cause of 21 of the deaths. Inquiry showed that the material was flannelette, winceyette, or cotton in 57 instances and victims wearing loose garments, such as nightdresses, skirts, or shirts, greatly outnumbered those wearing pyjamas. Of the 108 cases of scalding, 86 were in patients aged 4 years or under, 63 of whom were injured by upsetting containers of hot liquids, 8 had pulled over an electric kettle, 6 were scalded by too hot bath water, and 11 by falling into a bucket of hot water on the floor; a burst hot-water bottle was the cause in 4 cases. Of the total 25 deaths, 18 occurred in adults aged 60 and over, 5 in children aged between 5 and 8 years, while the remaining 2 were in patients aged 17 and 38.

The social survey showed that overcrowding existed in half the homes, being serious in one-quarter, and in the author's view is an important contributory factor in these accidents. The majority of patients came from the Registrar-General's Social Groups III, IV, and V. Replies to questions put to parents or patients in all social groups revealed marked ignorance of relevant legislation and of the dangers from inflammable fabrics, and revealed negligence in providing fireguards. A control group of parents of children under 6 years of age who had not been burnt were even less well informed and were equally negligent. The replies from three other groups of persons, namely, 50 State registered nurses, 64 medical students, and 25 recently qualified

doctors were alike disturbing. In a discussion of further legislation it is suggested that it might be useful to require the notification of all cases of burns and scalds to the local Medical Officer of Health who could then inspect the domestic heating arrangements and if necessary order the provision of fireguards; that all inflammable materials be labelled as such; that in council houses the kitchens should be better planned to minimize present hazards, and fireplaces should incorporate a fixing for the attachment of a fire guard. Above all, propaganda on a national scale is urgently needed and could be carried out by means of television and wireless programmes, leaflets at child-welfare centres, and instructions to old age pensioners; lastly, individual members of the medical profession could assist in the preventive work when occasion offered. *V. Reade*

1309. **The Behaviour and Educational Attainments of Deprived Children**
R. T. BEVAN. *Public Health* [*Publ. Hlth* (*Lond.*)] **69**, 234–237, June, 1956. 5 refs.

The behaviour, intelligence, and educational standard of 119 children born in 1940–1 who had been in the care of the local authority for varying periods of time, being either placed in homes or boarded out with foster parents, were studied. Each child had been taken into care for one of four main reasons—inability of an unmarried mother to support the child, failure of the parents to provide adequate care (usually owing to personality defects), loss by death or illness of one or both parents, and break-up of the home owing to parental disharmony.

Behaviour disorders, particularly aggressive or destructive behaviour and pilfering, were much more frequent in illegitimate children and in children whose parents were separated than in those deprived of parental care by death or illness or those whose parents had neglected them. The fact that behaviour disorders were more frequent in children in homes than those with foster parents is attributable to the high proportion of illegitimate and deserted children among the former. The incidence of abnormal behaviour was slightly higher among boys than girls, boys exhibiting more aggressive and violent forms of misbehaviour, whereas girls tended to show their maladjustment by shyness, sullenness, and disobedience. The assessment of scholastic progress disclosed (1) that 54·4% of the boys and 31·3% of the girls were more than 2 years retarded and (2) that those children who had been in care for the longest periods were the least retarded. *Franz Heimann*

1310. **Public Health Evaluation of New Housing in Moscow.** (Гигиеническая оценка нового жилищного строительства в Москве (период 1947–1951 гг.))
N. I. ANDREEVA. *Гигиена и Санитария* [*Gigiena*] 18–24, No. 6, June, 1956.

An investigation was carried out into living conditions in 18 blocks of flats erected in Moscow during the period 1947–51. Out of the total of 1,476 flats, a detailed examination was made of 353, with interrogation of 526 occupants. Of the flats examined, 45% housed one family and the remainder two or more. In 54% of cases the floor space per occupant was 6 sq. m., in 32% 6 to 9 sq. m., and in 14% more than 9 sq. m. Of the 667 families living in the 353 flats, 73% had but one room. In 90% of the kitchens the floor space was only 7 to 9 sq. m. Of the 353 bathrooms, 5 received direct daylight, 43 indirect light from the kitchen, and the remainder were artificially lit. The average floor space of lavatories was 1·26 sq. m.; 3 had direct lighting, 115 indirect, and the rest artificial lighting. The complaints recorded included: lack of courtyards for children; imperfect sound insulation between floors and between flats; kitchens inadequate for more than one family; lack of cupboards and storage space; absence of lifts in some 5- and 6-storey blocks; inadequate size of halls; noise and smell from refuse shoots and inadequate removal of refuse from the collecting chamber; and overcrowding. *R. Crawford*

1311. **Smallpox in Metropolitan France. Recent Epidemiological Lessons.** (La variole métropolitaine. Enseignements épidémiologiques récents)
R. CROSNIER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 2198–2203, June 22, 1956. Bibliography.

Several small outbreaks of smallpox have occurred in France during the last 15 years, the latest being at Vannes in the Morbihan *département* in 1955, when 16 out of 73 cases (22%) were fatal. A predominant feature of this outbreak, as of others, was the frequency of *formes frustes* in persons who had been vaccinated, 25 cases being characterized by the absence of an eruption, and the occurrence in 14 of these atypical cases of pulmonary complications associated with radiological changes in the lungs suggestive of either Loeffler's syndrome or a tuberculous infiltration. The author stresses the importance of vaccination and revaccination in the control of the disease and analyses possible untoward reactions which occurred during the epidemic in Marseilles in 1952. He concludes that vaccination or revaccination is absolutely contraindicated only in cases of coronary thrombosis, leukaemia, and diabetes, and emphasizes that despite the possibility of allergic reactions, general obligatory vaccination of the population is an essential measure of protection against epidemics of smallpox.

[See Leroux *et al.*, *Presse méd.*, 1955, **63**, 639; *Abstracts of World Medicine*, 1955, **18**, 518.]
Franz Heimann

1312. **Severe Localized Epidemic of "Infantile Paralysis" in the Tropics**
W. G. KERR and N. J. PEASE. *British Medical Journal* [*Brit. med. J.*] **1**, 1337–1340, June 9, 1956. 17 refs.

The north-western part of the Nzega District of Tanganyika has a population of about 100,000 Africans in an area of 1,000 square miles (2,590 square km.), which includes one township. The climate is subtropical and the sanitary conditions primitive. There are usually a few sporadic cases of infantile paralysis each year, but in September, 1954, the first cases in a severe localized epidemic were admitted to hospital, the epidemic continuing through the rainy months of November and December. The total number of cases

was 90, but a further 8 were notified in the next rainy season between March and May, 1955. The incidence was highest in the second year of life (36 cases); only 2 patients were over 5 years of age. Of the 79 cases admitted to hospital, 23 were severe (one fatal), and 15 very severe (10 fatal). The control measures included isolation of patients, improvement of general hygiene, and limitation of movement into and from the district. Of 46 patients traced and interviewed in July, 1955, 21 had recovered completely.

The authors suggest that this epidemic was caused by a strain of poliomyelitis virus of unusual virulence in a community with a high level of acquired immunity.

G. C. R. Morris

1313. **The Recovery of Poliomyelitis Viruses from Fecal Samples of Poliomyelitis Patients and Household Contacts**
C. A. MILLER and P. KAMITSUKA. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 607–615, June, 1956. 4 figs., 10 refs.

A study of household epidemiology of poliomyelitis is reported from the University of Kansas School of Medicine, Kansas City. The faeces of 192 persons from 35 households were examined for the presence of poliomyelitis virus by inoculation of roller tissue-cultures of monkey kidney cells. A stool specimen was regarded as negative only after at least two passages had yielded negative results. In each household one case of poliomyelitis had been diagnosed clinically, but only half of the total number of these patients had the paralytic form of the disease. In 9 households 21 contacts developed symptoms attributable to "minor illness", but none became paralysed; in the remaining households the contacts were symptom-free. Poliomyelitis virus was isolated from 34 out of 43 paralytic cases (including a number outside the households studied), from 26 out of 50 non-paralytic cases, from 12 out of 21 symptomatic contacts, and from 38 out of 113 symptomless contacts. The virus isolation rate declined sharply if the faeces were collected more than 3 weeks after the onset of symptoms. In one-third of all household contacts of a clinical case the stools yielded poliomyelitis virus. The virus carrier rate was much higher than this among (*a*) contacts who developed symptoms, (*b*) contacts of paralytic cases, and (*c*) contacts aged 10 years or under. In 80% of the contacts who were found to be infected with the virus no symptoms developed.

J. E. M. Whitehead

1314. **Evaluation of Canadian Poliomyelitis Vaccination Program, 1955**
E. H. LOSSING. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **47**, 104–110, March, 1956. 2 figs.

The efficacy of a campaign of poliomyelitis vaccination carried out in Canada in April, May, and June, 1955, was studied by comparing the attack rate in vaccinated children with that in unvaccinated children during the 5-month period July 1 to November 30, 1955. Cases of paralytic poliomyelitis only were included, and when possible the clinical diagnosis was confirmed by examination of stool specimens for the presence of the virus and estimation of the antibody titre in convalescent serum. A total of 589,716 children received two or more doses of vaccine during the 3 months to the end of June. The incidence of all forms of poliomyelitis in 1955 was exceptionally low—lower than in any of the preceding 10 years—and the total number of paralytic cases reported from January 1 to December 3 was 522, or 27% of the 5-year average of 1,893 cases.

Age-specific paralytic attack rates for 1955 and previous years were obtained from six provinces, and it was noted that rates for 1955 were substantially lower at all ages, the decline being more apparent in the younger age groups. In Prince Edward Island and in Nova Scotia, where the incidence was comparatively high in relation to the 5-year average (92% and 81% respectively), no paralytic cases were reported among 20,406 vaccinated children aged 5 to 8, whereas there were 13 cases among 52,089 unvaccinated children of comparable age, the difference being statistically significant.

It is concluded that in areas where the 1955 incidence was low a protective effect from the vaccine might be inferred, and that in areas where the 1955 incidence more nearly approached the 5-year average such an effect had been demonstrated.

F. T. H. Wood

1315. **The Distribution in England and Wales of Mortality from Coronary Disease**
W. J. MARTIN. *British Medical Journal* [*Brit. med. J.*] **1**, 1523–1525, June 30, 1956. 1 ref.

Between 1940 and 1954 the number of deaths from diseases of the coronary arteries occurring annually in England and Wales has risen from 10,648 to 41,688 for males and from 5,605 to 23,983 for females. The increase in the death rate from this cause in males has been more rapid than that in females at the younger ages, 35 to 54 years. The author quotes the study of Ryle and Russell (*Brit. Heart J.*, 1949, **11**, 370; *Abstracts of World Medicine*, 1950, **7**, 450) in support of the view that this rise in mortality cannot be accounted for by more accurate diagnosis or transference of deaths from other categories.

The standardized mortality ratio from coronary disease for males aged 35 to 64 in 1930–2 was 237 in Social Class I (professional) and fell progressively to 67 in Class V (unskilled labourers). The corresponding figures calculated from the 1% sample of the 1951 Census were 150 and 89 respectively, while for married women the order is reversed, the ratio in Class I being 92 and in Class V 108.

On comparison of standardized mortality ratios from coronary disease calculated for various regions and types of administrative area for 1950–2 the highest figures (for all types of area) were found in the northern regions and the lowest (for county boroughs and urban districts) in the midlands. The ratios for county boroughs were generally higher than those of urban or rural districts. The geographical differences cannot be explained by variations in the class structure of the population at risk. In each type of administrative area there was close correlation between standardized mortality ratios from coronary disease for males and females.

F. T. H. Wood

Industrial Medicine

1316. **Paralytic and Related Effects of Certain Organic Phosphorus Compounds**
W. F. DURHAM, T. B. GAINES, and W. J. HAYES. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 326–330, April, 1956. 19 refs.

From the laboratories of the U.S. Public Health Service, Savannah, Georgia, a method is described for testing in hens certain organic phosphorus insecticides for possible paralytic effects. The insecticide was administered in peanut oil by subcutaneous injection and observation was continued for 30 days.

Tri*ortho*cresyl phosphate (TOCP) and " isopestox " (" mipafox "; bis-*iso*propylaminofluorophosphine oxide) caused paralysis in 10 to 14 days. No delayed effects were seen after injection of " chlorthion ", " demeton ", " diazinon ", octamethyl pyrophosphoramide (OMPA), or O:O-demethyldichlorovinyl phosphate (DDVP). Malathion and EPN (O-ethylphenyl-*p*-nitrophenyl thiophosphonate) caused immediate leg weakness, the paralysis being localized and persisting after the acute cholinergic symptoms had subsided. With malathion the smallest dose to cause leg weakness was 100 mg. per kg. body weight and birds who survived the acute effects all made a complete recovery within 4 to 21 days. With EPN the smallest dose to cause muscle weakness was 40 mg. per kg. and in most cases the effects were irreversible.

It is noted, however, that judging by the results of earlier feeding experiments, EPN compares favourably with the toxicity of parathion and TIPP (tetra*iso*propyl pyrophosphate), while malathion appears to be among the safest, if not the safest, of these insecticides.

Reference is also made to the " ginger paralysis ", a condition which is due to the use of TOCP to fortify a ginger extract; the literature is reviewed.

M. A. Dobbin Crawford

1317. **The Pathogenesis of Disturbances of the Central Nervous System in Chronic Manganese Poisoning.** (Zur Pathogenese der zentralnervösen Störungen bei der chronischen Manganvergiftung)
J. PFEIFFER. *Archiv für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **14**, 408–427, 1956. Bibliography.

1318. **Inhalation Toxicology of Chlorine Trifluoride II. Chronic Toxicity**
H. J. HORN and R. J. WEIR. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 340–345, April, 1956. 3 refs.

The authors report that chronic exposure to chlorine trifluoride in a concentration of 1·17 p.p.m. was found to have severely toxic effects upon rats and dogs. Exposure for 6 hours a day, 5 days a week, for a period of 6 months caused pulmonary irritation in all the surviving rats; in 5 rats which died, and one accidentally killed pulmonary oedema and bronchopneumonia were present. The dogs were more severely affected, irritation of the upper respiratory tract proceeding to bronchopneumonia; in those which died multiple abscesses were found in the lungs post mortem. *M. A. Dobbin Crawford*

1319. **Chronic Toxicity of Aniline Vapor (5 ppm) by Inhalation**
F. W. OBERST, E. B. HACKLEY, and C. C. COMSTOCK. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 379–384, April, 1956. 1 fig., 28 refs.

In experimental studies which were carried out at the U.S. Army Chemical Center dogs, rats, mice, and guinea-pigs were exposed to an atmosphere containing aniline vapour in a concentration of 5 parts per million (19 mg. per c. metre) for 6 hours daily, 5 days a week, for 20 to 26 weeks.

No intoxication developed. The only sign of absorption in the dogs was an increase in the urinary excretion of chromogen. The rats showed a mild degree of cyanosis and methaemoglobinaemia towards the end of the experiment. It was calculated that the respiratory minute volume, in ml. per kg. body weight, was three times as great for the rats as for the dogs, so that the former were receiving three times as much aniline per unit weight as the dogs. By a similar calculation, for a man weighing 70 kg. the inhalation dosage per unit weight would be two-thirds that of a dog. The authors therefore conclude that 5 p.p.m. is a safe level for the maximum allowable concentration of aniline vapour in the working atmosphere. *M. A. Dobbin Crawford*

1320. **Arsine Poisoning**
D. B. MACAULAY and D. A. STANLEY. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **13**, 217–221, July, 1956. 1 fig., 8 refs.

1321. **Treatment of Lead Poisoning by Edathamil Calcium-Disodium**
D. O. SHIELS, D. L. G. THOMAS, and E. KEARLEY. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 489–498, May, 1956. 4 figs., 14 refs.

The sodium salt, tetrasodium ethylenediaminetetraacetate, has the property of forming with lead and other heavy metals compounds known as chelates, which are readily excreted by the kidneys. The calcium salt (edathamil calcium disodium) is less harmful than the sodium salt, because it does not remove calcium from body fluids and tissues. The authors describe the results obtained with oral administration—as opposed to the more usual intravenous injection—of edathamil calcium disodium in 21 cases of lead poisoning. The dosage was 2 g. twice daily for several days, followed by a

similar course after an interval of 7 days. There was a marked increase over pre-treatment values in both the concentration of lead in the urine and the total daily excretion in the urine—the concentration from 5 to 35 times and the total excretion from 5 to 22 times The amount of lead in the faeces was also considerably increased.

The concentration of lead in the blood varied at different stages of treatment, but the increase was generally only a fraction of the increase in the urinary concentration of lead. It is suggested that before treatment the various forms of lead in equilibrium are associated chiefly with the erythrocytes and proteins; when the equilibrium is disturbed by edathamil calcium disodium the chelate formed is a much smaller molecule of lead proteinate, which is able to pass readily into the glomerular filtrate. The fact that the amount of lead eliminated during treatment was much greater than that estimated to be circulating in the blood before treatment was begun would suggest that there had been considerable clearing of lead from organs and tissues, and it is probable that a large proportion of this came from the bones.

Subjective symptoms of fatigue, weakness, and loss of appetite improved by the second or third day, but not more rapidly than when sodium citrate or sodium thiosulphate was given in treatment. Colic was also relieved, but as some patients had also received calcium gluconate or pethidine the efficacy of edathamil calcium disodium in this respect was difficult to assess. No serious untoward effects were noted. In 2 cases ultimate recovery was more rapid, and the increase in the urinary excretion of lead over a given period of time was much greater, with this drug than with sodium citrate.

Ethel Browning

1322. **The Industrial and Experimental Pathology of Tetryl: Experimental Researches, Clinical Observations, and Prevention.** (Patologia professionale e sperimentale da tetrile: ricerche sperimentali, osservazioni cliniche e prevenzione)

L. Parmeggiani, E. Bartalini, C. Sassi, and A. Perini. *Medicina del lavoro* [*Med. d. Lavoro*] **47**, 293–313, May, 1956. 6 figs., 26 refs.

In an investigation undertaken at the University of Milan into the clinical aspects of occupational disease due to tetryl 220 workers of both sexes in a factory making explosives, all but 84 of whom had worked there for more than 6 months, were kept under close clinical observation for 2 years. Contrary to the experience of others, the authors found that the occurrence of symptoms was directly related to the intensity of exposure to tetryl, and that in very dusty working conditions they might appear within 3 to 4 days of starting work, such disturbances being due not to allergy, but to cumulative toxic action.

The symptoms and clinical findings encountered are discussed, with special reference to dermatitis. This usually presented as an erythema with more or less extensive foci on the neck, chest, back, and flexor surface of the forearms, but occasionally it was vesicular. These foci generally disappeared after a few days, with subsequent slight desquamation; in only 3 out of 37 cases was removal from work necessary. Among the general symptoms, headache was chiefly frontal and tended to increase with each day of exposure until it was relieved by epistaxis, which was a prominent feature; it is attributed to a direct effect of tetryl powder on the nasal mucosa. Disturbances of the digestive system were relatively frequent, diarrhoea being the principal symptom, and were relieved within 2 days of removal from contact with tetryl; more than 10% of their subjects were affected. Symptoms referable to the central and vegetative nervous systems occurred especially in females, and included erethism, insomnia, nocturnal agitation, sweating, and anxiety states; the reflexes were exaggerated, with or without tremor of the outstretched fingers. Women workers complained of increased frequency of the menses while working with tetryl. Examination of blood films showd no toxic granules in the leucocytes and no Heinz bodies, examination of the urine for picric and picramic acids was negative, and electrophoresis of the serum revealed no abnormality.

In controlled experiments on rats which were fed with varying amounts of tetryl for different periods the kidney tubules were found to be principally affected, followed by the liver parenchyma. In rabbits given subcutaneous injections of tetryl in propylene glycol the findings were similar, with severe local damage at the site of injection as well.

Improvements in the methods of working are recommended so as to reduce the tetryl content of the atmosphere to 1 mg. per c. metre, which is regarded as the maximum allowable level. The use is advised of properly fitting overalls, sleeves, suitable head coverings, and barrier cream, with regular bathing with an indicator soap made up with sodium sulphite. The use of masks is not advised. During the 2 years of this study the concentration of tetryl in the atmosphere of the factory concerned had been reduced from 2·6 to less than 1 mg. per c. metre.

W. K. Dunscombe

1323. **Occupational Disease in a Chromate Factory.** (La patologia professionale in una fabbrica di cromati)

C. Sassi. *Medicina del lavoro* [*Med. d. Lavoro*] **47**, 314–327, May, 1956. Bibliography.

The author reviews the literature of chromate poisoning and discusses the chemistry of chromic acid and its various salts and then describes the results of an investigation carried out at the University of Milan over a period of one year in which 65 men working in one part of a factory producing chromic acid and bichromates were kept under observation, periodic estimations of the atmospheric chrome content at various sites being made. The ages of 54 of the workers were between 36 and 60 years, and more than half of the group had been employed on this work for less than 10 years.

In view of the notorious frequency of ulceration of the skin in chrome workers it is interesting to note that only 4 out of the 65 had cutaneous lesions, whereas no less than 32 had perforation of the nasal septum and a further 6 atrophy and ulceration of the septum. The perforations were completely painless. Gastric or duo-

denal ulcer was present in 10 cases, and symptoms referable to the liver and biliary system in 15. The chest radiograph was normal in all cases, as also was the electrocardiogram. The urinary excretion of chromium was tested in 25 cases and was relatively high, the amounts absorbed appearing to bear a close relation to the chrome content of the atmosphere. There was a slight hypochromic anaemia in most cases. A variety of liver function tests were performed and mostly showed little abnormality, though tests of serum lability (Takata, Uncko, Kunkel, and others) gave slightly positive results, suggesting that chrome may have some pathological action on the liver.

No investigation into the cause of death among workers who had left the factory was practicable, but of 3 deaths among the workers under observation, one was due to an accident, one to a squamous-celled carcinoma of the nasal septum, and one to a small-celled invasive tumour of the lung. The possible relation of these tumours to exposure to chrome is discussed.

In view of the very high incidence of septal ulceration and of other conditions of the upper respiratory passages found in this investigation, the author considers that the maximum allowable concentration for chrome should certainly be less than the accepted standard of 0·1 mg. per c. metre and preferably not more than half this figure. *W. K. Dunscombe*

1324. **Recent Observations on Pneumoconiosis Due to Diatomaceous Earth.** (Observations récentes sur la pneumoconiose par terre à diatomées)
P. Luton, J. Champeix, M. Ravet, and A. Vallaud. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **17**, 125–148, March–April, 1956. 5 figs., 9 refs.

Previous French observations on workers exposed to the dust of diatomaceous earth have suggested that there was less disease than would have been expected from the intensity of exposure and the silica content of the dust. However, the notification of several cases of silicosis arising in factories where diatomaceous earth was calcined threw doubt on this opinion and led to the present investigation. The authors express the hope that their present paper may draw attention to the risks to which workers may be exposed in such factories and to the means of protecting them.

Three factories in central France, designated A, B, and C, were investigated. At A the diatomaceous earth was dried at 400° C., but not calcined; at B it was calcined at 800° C.; and at C, a new factory, it was dried and then calcined at 900° C. in the presence of sodium chloride. *X*-ray analysis of the products showed a small transformation of amorphous silica to cristobalite at A, a partial transformation at B, and almost complete transformation at C. Dust counts carried out on samples collected at C on a filter and then dispersed in water showed an atmospheric concentration ranging from 90 to 24,000 particles per ml.

At Factory A there were 6 cases of silicosis (dust exposure 6 to 18 years) among 30 workers, at B there were 3 cases (dust exposure 7 to 26 years) among 12 workers, and at C 10 cases (dust exposure 1 to 4 years) among 120 workers, including 2 fatal cases in which the period of exposure was 22 and 30 months respectively. It is concluded that at Factory C exposure to dust with a high cristobalite content, possibly aggravated by exposure to hydrochloric acid from the calcining process, was producing a severe risk of silicosis arising after relatively short exposure.

The problems of prevention both by dust suppression and by medical supervision are discussed in detail. The enforced wearing of effective masks in certain parts of the factory and 6-monthly *x*-ray examination are suggested. *C. M. Fletcher*

1325. **Death Rates of Miners and Ex-miners with and without Coalworkers' Pneumoconiosis in South Wales**
R. G. Carpenter and A. L. Cochrane. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **13**, 102–109, April, 1956. 16 refs.

This paper from the M.R.C. Pneumoconiosis Research Unit is a study of the death rates in the whole population of the Rhondda Fach, a coal-mining valley in South Wales with a population of about 30,000, over an average period of 2·6 years. Approximately 90% of the population over the age of 5 years had undergone chest radiography at the beginning and end of the study period. The observed numbers of deaths in males and females of different age groups, in miners and in non-miners, and in persons placed in different radiological categories of pneumoconiosis (employing for this the international system of classification) are compared with the numbers to be expected from the Registrar-General's figures for England and Wales as a whole.

Although the numbers of deaths were too small for the mortality from separate causes to be examined, some interesting conclusions are reached, of which perhaps the most important is that there was no evidence that simple pneumoconiosis was associated with any decreased expectation of life. In addition there was " only suggestive evidence that progressive massive fibrosis is a lethal disease ". *John Pemberton*

1326. **Industrial Hygiene in Relation to the Manufacture of Fluorescent Lamps.** (Вопросы гигиены труда в производстве люминесцентных ламп)
E. I. Gol'dman. *Гигиена и Санитария* [*Gigiena*] 33–40, No. 6, June, 1956. 6 refs.

The technical processes in the production of fluorescent lighting tubes involving contact with beryllium, silica, wolfram, lead, manganese, mercury, and other substances, are detailed. Recommendations are made for the protection of the workers' health, including improvements in luminophore production techniques, particularly in relation to the grinding, sieving, mixing, and calcining processes, the use of improved methods for the exhaustion and filling of lamps with mercury vapour, and for dealing with rejected tubes, the segregation of dangerous processes, and the use of gloves, barrier creams, and other measures of personal hygiene. The periodic examination of workers in this industry is advised. *R. Crawford*

Forensic Medicine and Toxicology

1327. **Sudden and Unexpected Death in Infancy and Childhood**

L. ADELSON and E. R. KINNEY. *Pediatrics* [*Pediatrics*] 17, 663–699, May, 1956. 24 figs., bibliography.

Under the auspices of the U.S. Public Health Service an investigation was carried out at the Western Reserve University School of Medicine, Cleveland, Ohio, into the causes of sudden and unexpected death occurring in infants and children between the ages of 10 days and 2 years. All such cases certified during a 2-year period by the Coroner's Office of Cuyahoga County (population approximately 1,600,000) were studied, the total being 126, together with a control group of 16 children of similar age who died rapidly as a result of violence. In every instance a most careful necropsy was performed, material being taken from many sites for histological and bacteriological investigation, while at the same time a sociological survey of the house and family was made.

No less than 85% of the children dying unexpectedly were under 7 months old. The sexes were equally represented, but the proportion of negroes was nearly double that in the general population. In no instance had symptoms been noted for more than 48 hours before death, though in some cases interrogation of the parents showed, and the necropsy confirmed, that signs and symptoms consistent with "dangerous illness" [not further defined] had been present, though unrecognized. In 99 cases the infant was found dead, but in the remaining 27 the agonal stages and death were witnessed, so that the possibility of suffocation by bedclothes or overlaying could be excluded. Nevertheless, the post-mortem appearances regarded as pathognomonic of mechanical asphyxia, such as cyanosis, fluidity of the blood, pulmonary congestion, and petechiae, were found just as frequently in these 27 cases as in those in which death was unobserved.

Among the more remarkable findings the following are worthy of mention. (1) In more than 83% of cases there was evidence of inflammation of varying degrees of severity in the respiratory tract, and acute haemorrhagic pulmonary oedema was frequently present. (2) There was an almost total lack of anything suggestive of "status lymphaticus" or any other of the abnormalities of the spleen, thymus gland, or lymph nodes to which sudden death in infancy was often attributed in the past. (3) In only 3 cases could overlaying have been a major factor, though in all 3 a moderately severe infection of the respiratory passages was also present and it was impossible to state which was the primary cause of death. (4) Although in a number of cases the pillow or bedclothes were stained with sero-sanguineous fluid or gastric contents, in none of these was there any evidence that death was due to mechanical asphyxia, necropsy showing that pulmonary infection or acute haemorrhagic pulmonary oedema, or both, was present in each case. (5) In a number of cases unsuspected congenital abnormalities were discovered, but of 4 children with congestive failure associated with congenital heart disease, only one was free from inflammatory changes in the respiratory tract.

Despite the high incidence of inflammatory changes in the respiratory tract, bacteriological investigation failed to reveal consistently any organism or group of organisms of aetiological significance in the lungs, and blood culture was usually negative. Moreover, comparable inflammatory changes were noted as incidental findings in certain control subjects, showing that such changes are not necessarily lethal. The exact mechanism of death in these cases is therefore not apparent from the respiratory findings, and a number of possible explanations are discussed. The authors emphasize that although it has been demonstrated that mechanical asphyxia by bedclothes is rarely responsible, no statement as to the cause of death in an infant who has died suddenly should be made without complete investigation.

[The medico-legal implications of this paper are of the greatest importance and the abstracter knows of no comparable series in which such exceptionally detailed investigations have been made. The paper deserves to be read in full, as no abstract could possibly do it justice.]

W. K. Dunscombe

1328. **Lightning Accident at Ascot**

G. P. ARDEN, S. H. HARRISON, J. LISTER, and R. H. MAUDSLEY. *British Medical Journal* [*Brit. med. J.*] 1, 1450–1453, June 23, 1956. 9 figs., 5 refs.

The circumstances and effects of a thunderstorm which broke over the racecourse at Ascot, Berkshire, in July, 1955, are described. A considerable number of people were thrown to the ground, and 46 were taken to hospital. Twelve of the patients were rendered unconscious for more than a few minutes, and 2 of these died from head injuries. Many had retrograde amnesia and many who were momentarily dazed found that they could not move their limbs or rise from the ground. Paraesthesiae in the limbs were commonly reported. In most of the patients the neurological disturbances cleared up completely. Of the total number admitted to hospital, 15 suffered from burns, which presented the characteristics usually observed in cases of lightning stroke, including feathering, erythema and blistering, punctate full-thickness skin loss, linear charring, contact burns from metal, and flash burns. In one case the eardrums were ruptured, the appearances closely resembling those seen after a bomb explosion; there was residual partial deafness in this case. A boy of 10 suffered transient eye damage similar to that seen in the eyes of arc welders.

The literature on the effects of lightning stroke is reviewed.

Gilbert Forbes

Anaesthetics

1329. **An Innovation in Technique f or Dental Gas**
A. Tom. *British Medical Journal* [*Brit. med. J.*] **1**, 1085–1087, May 12, 1956. 1 ref.

The author reports good results with a new dental gas technique—" amnalgesia "—first described by Klock (*Curr. Res. Anesth.*, 1955, **34**, 379), which he has now used in 200 cases, mostly in children at school dental clinics in Gloucestershire. No premedication is given; the patient is settled in the dental chair, the machine is set to deliver nitrous oxide " just off the pressure flow ", a suitable sized nose-piece is put in position, and the patient told to blow into it through his nose. After 2 breaths the pressure is slightly increased and the breathing bag switched into the circuit. After four more breaths the machine is set to 15% oxygen (or to 20% for children aged over 13 and adults). Thereafter it takes about forty breaths to secure the condition of amnalgesia, which is recognized by the breathing becoming a little hesitant; this must be corrected by exhorting the patient to keep blowing through the nose, or the mouth may be covered with the hand for a few breaths. Usually the breathing then becomes free and regular, but it is not automatic and not stertorous. The eyelids are relaxed and the eyes lose expression and begin to roll; the patient's colour is bright pink. Extractions can now be begun. Any reversion to mouth-breathing must be countered by temporarily reducing the proportion of the oxygen by 2% until dental operations permit the mouth being covered for a few moments.

The author states that induction takes slightly longer than by normal methods, but anaesthesia is smoother and operating conditions better. There is never any hypoxia, and gagging and swallowing reflexes are not abolished—an added safety factor. The method can be used for children as young as 3 years or so. The importance of maintaining nasal breathing is stressed. Any tetanic or convulsive movement (as distinct from a voluntary movement) must be met with an increase in the percentage of oxygen. In all the author's cases recovery was uneventful and the patient had apparently no memory of experiencing any pain or knowledge of extraction. *W. Stanley Sykes*

1330. **Effects of Mephentermine Sulfate as a Prophylactic Vasoconstrictor for Spinal Anesthesia**
B. M. Anderson and P. Matzinger. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **35**, 234–241, May–June, 1956. 3 refs.

The vasoconstrictors usually administered during spinal analgesia lose their effect with repeated doses. Ephedrine and " methedrine " (methylamphetamine) cause cerebral stimulation, " vasoxyl " sometimes gives rise to bradycardia, while the margin between the therapeutic and the toxic doses of " neosynephrine " (phenylephrine) is very narrow. At the Samuel Merritt Hospital, Oakland, California, a new pressor substance, mephentermine sulphate, was given to 367 patients aged 15 to over 80—for pelvic surgery in 182 cases, upper abdominal operations in 26, and extra-abdominal operations in 159. An initial dose of 30 mg. was given in 251 cases and one of 45 mg. in the rest. The basal blood pressure was the average of two readings from the patient's chart and one taken in the operating theatre. If the systolic blood pressure fell by more than 20 to 60 mm. Hg after the anaesthetic was given, additional doses of mephentermine were administered.

If the drug was given immediately before the spinal injection hypotension did not develop during analgesia. The maximum effect of the initial dose was achieved in 20 minutes. The efficacy of mephentermine was about the same whether the drug was given intramuscularly or infiltrated with the procaine subcutaneously at the site of the spinal puncture. In 78% of the 367 cases the initial injection was sufficient to maintain the blood pressure; in 19% one additional dose was necessary, and in 3% (operations lasting 2 hours or more) 2 additional doses were required. At no time was there any evidence of cerebral stimulation or disturbance of cardiac or respiratory function.

The authors state that the optimum dose of mephentermine is probably about 35 mg. For active treatment of hypotension it should be given intravenously in doses of 15 to 30 mg. *W. Stanley Sykes*

1331. **Long-term Follow-up of Patients who Received 10,098 Spinal Anesthetics. Syndrome of Decreased Intracranial Pressure (Headache and Ocular and Auditory Difficulties)**
L. D. Vandam and R. D. Dripps. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 586–591, June 16, 1956. 18 refs.

The headache that frequently follows spinal anesthesia is sometimes associated with visual and auditory difficulties and dizziness. This syndrome was studied in connection with 9,277 anesthetizations by the spinal technique, and the data were compared with those from 1,000 other patients who were given general anesthesia over the same period of time.

The over-all incidence of the headache, which occurred in 9,277 anesthetizations, was 1,011, or 11%. The oldest patients were least susceptible to it, and men were less susceptible than women. Its incidence when needles of small diameter were used was much less than that with needles of large diameter; the 22-gauge needle was found best for routine use. Headache could be virtually eliminated by the employment of a 24-gauge needle. The data on duration and time of onset of the headache, on the effects of postural changes, and on the visual and auditory phenomena indicate that this syndrome results from a decrease in cerebrospinal fluid pressure and that the decrease is caused by leakage of the fluid.—[Authors' summary.]

1332. **Treatment of Adrenal Cortical Insufficiency during Surgical Procedures**

W. S. Howland, O. Schweizer, C. P. Boyan, and A. C. Dotto. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1271–1273, April 14, 1956. 1 fig., 9 refs.

During a period of one year 25 patients, or approximately one in every 300, subjected to operation at the Memorial Center for Cancer (Cornell University), New York, showed signs of adrenal cortical insufficiency, such as hypotension persisting despite transfusion and the administration of vasopressor drugs, depressed respiration, or delayed emergence from anaesthesia. These signs were found most frequently in the elderly, the chronically debilitated, the morbidly nervous, and in patients with disease or absence of the adrenal glands. The treatment recommended is the intravenous infusion of 100 mg. of hydrocortisone dissolved in 500 ml. of saline or 5% dextrose solution. The histories are appended of 7 cases in which acute adrenal insufficiency supervened during or after anaesthesia and was successfully treated in this way.

The mechanism of action of hydrocortisone is uncertain. However, adrenal cortical hormones are known to be necessary for the maintenance of peripheral vascular tone, and any hypotension which occurs as a result of shock will diminish cortical activity by reducing the blood flow to the adrenal glands, causing acute cortical deficiency. *Mark Swerdlow*

1333. **Cardiac Arrest**

T. H. Hewlett, C. W. Gilpatrick, and W. F. Bowers. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **102**, 607–615, May, 1956. 3 refs.

In this paper from the Brooke Army Hospital, Fort Sam Houston, Texas, the features of cardiac arrest and its treatment in 28 cases occurring in a 5-year period are discussed. Of the 28 patients, 10 were children aged 3 weeks to 11 years; 8 of these were classified as poor-risk patients with chronic anoxia as a primary clinical feature, while 6 had congenital heart disease. Significant factors contributing to arrest, including anoxia, circulatory deficit, or toxaemia, were present in 7 patients before induction of anaesthesia and appeared during induction in 2. The condition developed during operation in 8 of the 10 cases, during induction in one, and during the postoperative period in one, arrest occurring in 8 patients and ventricular fibrillation in 2. Treatment was by cardiac massage. One patient survived without sequelae.

Of the 18 adults, aged 15 to 68 years, 13 were poor-risk patients. Chronic anoxia was a significant factor of the primary disease in 13 cases, 8 of which were considered " hopeless ". Factors favouring cardiac arrest were present before induction in 12 cases and were manifest in the operating theatre in 3. Arrest developed during induction in 4 cases, during operation in 10, postoperatively in 3, and during tracheal aspiration in one case. No general anaesthetic was given in 2 cases. The cardiac arrest was initiated by many factors, including sudden haemorrhage, intracardiac manipulation, tracheal stimulation, position change after blood loss, and acute hypoxia. Treatment was by cardiac massage through the 4th or 5th left interspace without opening the pericardium initially. To aid weak contractions 1 to 2 ml. of a 1-in-10,000 solution of adrenaline was given directly into the ventricular chamber and in the case of a flabby heart 5 to 10 ml. of 1% calcium chloride solution was given. Defibrillation was used in ventricular fibrillation if massage was not rapidly effective. Of the 18 patients, 12 were resuscitated and 7 of these made a complete recovery, although one patient sustained temporary cerebral damage.

The authors emphasize the need for rapid diagnosis and treatment and for immediate access to sterile instruments and electrodes. They discuss the type of patient with chronic anoxia due to any cause in whom cardiac arrest is likely to occur, and the prevention of this catastrophe by careful preoperative preparation. Initiating factors seem to be acute anoxia and vagal reflexes. *Raymond Vale*

1334. **Cardiac Arrest. Study of a Thirty-year Period of Operating Room Deaths at Massachusetts General Hospital, 1925–1954**

B. D. Briggs, D. B. Sheldon, and H. K. Beecher. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1439–1444, April 28, 1956. 2 refs.

A study of the records of 189,815 operations performed during the last 30 years at Massachusetts General Hospital, Boston, showed that the incidence of cardiac arrest had increased, the incidence for the 10 years 1925–34 being 1 in 1,518 as compared with 1 in 1,038 for the decade 1945–54. Cardiac arrest was far commoner in older patients than in younger ones—but the proportion of old people subjected to surgery increased. Again, cardiac arrest was more common in patients in poor physical state than in those in good condition. The incidence was also higher in patients with pre-existing heart disease than in those without; however, it is generally agreed that surgery is now withheld from fewer patients with heart disease than was the case in the early part of the period under review.

The authors state that it is usually impossible to determine the exact cause of cardiac arrest. A more or less rapid increase in the depth of anaesthesia was the commonest associated factor, but three-quarters of the patients in this group recovered. In 6 instances the associated factor was reflex activity; all these patients recovered. Hypoxia was responsible in 13 out of 100 cases with recovery in 4, and pre-existing heart disease in 16 with recovery in 3. The importance of speed in treatment is emphasized by the fact that neurological sequelae were observed in all patients in whom cardiac action was restored when thoracotomy was delayed more than 4 minutes.

The figures suggest that the increased incidence of cardiac arrest is not due to bad practice, and this is borne out by the fact that the condition is successfully treated in many more cases today than formerly; during the last 10 years the recovery rate has been 37% and in the last 5 years 50%. *Ronald Woolmer*

Radiology

RADIODIAGNOSIS

1335. **The Genetically Significant Radiation Dose from the Diagnostic Use of X Rays in England and Wales. A Preliminary Survey**
S. B. OSBORN and E. E. SMITH. *Lancet* [*Lancet*] **1**, 949–953, June 16, 1956. 23 refs.

The authors have attempted to ascertain whether or not the number of genetic mutations induced by exposure to ionizing radiations for diagnostic purposes is significant. For this purpose they have assumed that the number of radiation-induced mutations added to the population at the birth of a child is proportional to the total radiation dose received by the gonads of both parents from the time at which each one of them was conceived up to the time at which the child was conceived.

It is estimated that approximately 17,660,000 *x*-ray examinations were performed in England and Wales during 1954, and that 7,720,000 of these were carried out on persons under the age of 30. The age and sex distribution of the patients and the proportions of different types of examination were calculated from an analysis of the work of 5 representative hospitals (giving a 1-in-800 sample of the annual total of examinations). By reference to population statistics it is possible to estimate the risk in subsequent parenthood at any given age, and the average dose accumulated by the gonads up to that age was weighted in accordance with that risk. The weighted dose ("genetically significant radiation dose") is then expressed in terms of a new unit which the authors call the "roentgen-equivalent-genetic" or "reg". Calculations based on the minimum dosage likely to be received by the gonads during diagnostic examinations suggest that diagnostic radiology contributes an increase of at least 22% over the dose due to natural radiation and that such increase may well be several times greater than this figure. The authors consider that it is "not impossible" that this constitutes an appreciable genetic hazard to the population as a whole.

Of the various types of *x*-ray examination, a few—notably examination of the hip and lumbar spine, pyelography, and pelvimetry—although they constitute only 7% of the total examinations, contribute nearly three-quarters of the total of genetically significant radiation, while faulty radiographic technique may increase this dose.

G. Ansell

1336. **A Controlled Study of Cortisone Therapy for Headache after Pneumoencephalography**
O. A. FLY, C. S. MACCARTY, R. P. GAGE, H. N. MACKINNON, and P. H. JONES. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 415–418, June 2, 1956. 9 refs.

1337. **Roentgenologically Demonstrable Gastric Abnormalities in Cases of Previous Congenital Pyloric Stenosis.** [In English]
O. S. NIELSEN and M. ROELSGAARD. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **45**, 273–282, April, 1956. 7 figs., 9 refs.

In a previous paper (*Acta paediat.* (*Uppsala*), 1954, **43**, 432; *Abstracts of World Medicine*, 1955, **17**, 456) the first-named author described a follow-up study of 95 out of 136 surviving patients who had been medically treated for severe congenital pyloric stenosis in two Danish hospitals in the period 1907–27. This showed that of the 95 patients, 27 had symptoms of ulcer or gastritis, as compared with 12 in a control group of similar age and sex. The authors now report from the County Hospital, Gentofte, Copenhagen, the results of barium-meal examination of 19 of the 27 with symptoms and 26 of the 68 who were symptom-free. [Since the 37 men and 8 women, most of whom were aged between 25 and 45, are not considered separately it must be assumed that age and sex had no relation to the findings.]

Radiological evidence of the earlier pyloric stenosis was found in 35 patients, of whom, however, 22 had no symptoms, although 3 had peptic ulcer, while no such evidence was found in 10 patients, of whom 4 had no symptoms but 2 had peptic ulcer. Of the 19 patients with symptoms, 9 had peptic ulcer. Thus, neither peptic ulcer nor symptoms were particularly associated with the persistent pyloric narrowing. Peptic ulcer was in fact markedly less common in the cases with sequelae (8 out of 35) than in the cases without sequelae (6 out of 10). The cause of the high incidence of peptic ulceration (14 out of 45 cases) remains unexplained.

[None of the original 95 patients seems to have undergone gastrectomy and there is no mention of the frequency of gastrectomy in the general population.]

Denys Jennings

1338. **Duodenal Loop Changes in Posterior Penetration of Duodenal Ulcer**
J. G. TEPLICK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 958–974, May, 1956. 12 figs., 7 refs.

The author describes the radiological findings in the duodenal loop in 10 cases seen at Kensington Hospital, Philadelphia, between 1947 and 1953 in which the evidence pointed to posterior penetration of a duodenal ulcer. Of the 9 cases confirmed at operation (the 10th patient refused surgery) the ulcer penetrated into the pancreas in 6, necessitating partial pancreatectomy in 2; in the other 3 cases the *x*-ray findings were explained by the presence of dense adhesions to the pancreatic bed. The constant sign was a "somewhat stiff appearance", which was caused by the absence of valvulae conniventes on the inner side of the descending duodenal limb. Sometimes the descending limb was also displaced back-

wards and to the right and the mucosal folds were coarsened. There tended to be a long history of severe symptoms, but in 4 of the cases there was no radiation of pain to the back. The author suggests that the presence of these radiological signs may help a clinician to decide in favour of operation in a condition for which purely medical treatment has little to offer.

Denys Jennings

1339. **The Roentgen Manifestations of Pulmonary Hypertension in Congenital Heart Disease**
T. E. KEATS, V. A. KREIS, and E. SIMPSON. *Radiology* [*Radiology*] **66**, 693–700, May, 1956. 4 figs., 16 refs.

Thirty-six cases of proved pulmonary hypertension associated with interatrial septal defects, interventricular septal defects, or with patent ductus arteriosus were reviewed in an attempt to determine if the criteria established for the roentgen detection of pulmonary hypertension in mitral valvular disease could be applied also in congenital heart disease. The only one of these criteria which proved applicable was disproportionate narrowing of the peripheral pulmonary arteries as compared to the proximal arteries. This sign was present in 64% of the series studied. The other reported signs of right ventricular and pulmonary outflow tract enlargement occur in the presence of left-to-right shunts without pulmonary hypertension and are, therefore, unreliable as indicators of the presence of pulmonary hypertension. The degree of enlargement of the heart, right ventricle, and the pulmonary artery appears to correlate more closely with the magnitude of pulmonary blood flow.—[Authors' summary.]

1340. **Amyloid Disease. Its Roentgen Manifestations**
C. C. WANG and L. L. ROBBINS. *Radiology* [*Radiology*] 66, 489–501, April, 1956. 15 figs., 13 refs.

Between 1945 and 1954 at the Massachusetts General Hospital, Boston, 29 cases of amyloid disease came to necropsy. The radiographs in 19 of these cases and those of 2 additional cases seen elsewhere have been studied, the findings being discussed in the present paper. The condition was primary in 8 of the 31 cases, secondary in 20, and associated with multiple myeloma in 3. Secondary amyloid disease was associated with rheumatoid arthritis in 10 of the 20 cases, and in the remainder with Hodgkin's disease, tuberculosis, bronchiectasis, or ulcerative colitis. In three-quarters of the cases amyloid was found in the kidney and spleen.

In 5 out of 7 cases with amyloid in the spleen there was radiological evidence of moderate splenomegaly. When the kidneys were chiefly involved enlargement was accompanied by functional impairment without distortion of the collecting system. In the early phases of the disease the lungs showed no radiological abnormality. In 6 out of 9 cases of pulmonary amyloid there was increased prominence of the bronchovascular markings and slight stippling in the peripheral lung fields. In the late stages the appearances were those of a miliary process and in severe cases they simulated lymphatic spread of a malignant growth. Massive infiltration of the heart produced gross enlargement followed by congestive failure. The gastric manifestations of amyloid disease consisted in ulceration, thickened gastric rugae with decreased motility and flexibility, and tumour formation. In 5 of the cases with amyloid disease secondary to rheumatoid arthritis gastric ulceration was found. The authors state that the exact relationship, if any, between amyloid disease and peptic ulceration is obscure. Severe amyloid disease in the small intestine resulted in impaired motility and ileus. It was difficult to determine whether thickening of the mucosal folds seen in the large intestine was due to amyloid deposit or submucosal haemorrhage, or both.

It is pointed out that the changes noted in the various organs are not pathognomonic of amyloid disease. The recognition of primary amyloidosis is difficult, but the diagnosis may be suggested by the radiological appearances and confirmed by tissue biopsy.

John H. L. Conway-Hughes

1341. **Ewing's Sarcoma: its Roentgen Classification and Diagnosis**
R. S. SHERMAN and K. Y. SOONG. *Radiology* [*Radiology*] **66**, 529–539, April, 1956. 13 figs., 22 refs.

The radiological appearances in Ewing's sarcoma of bone were studied from the records of 111 cases seen at the Memorial Center, New York. Of the 111 patients (77 males and 34 females), 47 were between 10 and 19 years of age, only 5 being over 30 and 4 under 2 years. In none of the cases was a primary tumour encountered in the skull, vertebrae, or mandible, although metastases were found in all parts of the skeleton. The tumours most frequently occurred in the long bones, the femur being the commonest site, followed by the pelvis and ribs, in that order. While there was great variation in the radiological appearances of the long bones, a similarity was noted among tumours in the same location which justified classification as follows: (1) diaphysial —central and cortical; and (2) metaphysial—central, peripheral, and epiphysial.

Central diaphysial tumours, usually regarded as the classic type, constituted almost half the long-bone tumours. The typical radiological features were involvement of about one-third of the shaft, fusiform configuration, frequent involvement of soft parts, fine patchy internal pattern of bone destruction, ill-defined edges, and a parallel form of periosteal reaction. Pathological fractures were found in 8 out of 29 cases and occurred subsequently in 4. In about 50% of cases perpendicular periosteal spiculation was noted in addition to the laminated form. The most characteristic features of cortical diaphysial tumours were erosion of the outer surface of the cortex and a large extra-osseous tumour. The tumours were found at or near the midshaft level and were asymmetrical. Pathological fracture was not encountered.

Central metaphysial tumours were found in 6 cases; these were symmetrically placed and pear-shaped. In 5 cases the epiphysis was not closed. Sclerosis was seen in addition to patchy bone destruction. Peripheral metaphysial tumours, which simulate osteogenic sarco-

mata, were present in 10 cases, and metaphysial–epiphysial tumours in 6. Of the latter group the epiphysial line was closed in 5; there was, however, no clear-cut example of epiphysial involvement alone.

In 2 cases tumours were found in small tubular bones, one being of the central diaphysial type and the other of the central metaphysial type. The most striking feature of Ewing's tumour in the rib, of which there were 16 cases, was a spherical, intrathoracic mass of the density of water associated with the lesion. In most instances there was no periosteal reaction on the outer surface of the bone, and one-fourth to one-third of the rib length was involved. In 13 of the cases the tumour was predominantly lytic.

Tumours occurring in the flat bones presented no special appearances which could be relied upon for identification. Metastases were common in other bones and tended to simulate the primary growth, making differentiation difficult. Metastases in the lungs occurred in about two-thirds of the cases, and were characterized by multiple nodules of varying size. There was a good response to irradiation, the effects of this treatment—diminution of the soft-tissue mass, fresh spicule formation which later fused to form new bone, and repair of the internal bone pattern without scarring—being visible radiologically about one month afterwards. The authors emphasize that less than 25% of cases present the classic appearances of Ewing's sarcoma, and that the radiologist is therefore seldom justified in making this the sole diagnosis. *John H. L. Conway-Hughes*

RADIOTHERAPY

1342. **The Value of Radiation Therapy in the Management of Glioma of the Optic Nerves and Chiasm**
J. M. Travers, L. A. Mount, and E. H. Wood. *Radiology* [*Radiology*] **66**, 518–528, April, 1956. 4 figs., 17 refs.

At the Neurological Institute, New York, 34 cases of primary glioma of the optic nerves and chiasm occurred during a period in which approximately 2,000 cases of glioma of all types were encountered. The diagnosis was established by histological examination of the lesion in 19 cases, by surgical gross inspection of the lesion in 6 cases, and by clinical and radiological methods in 9. The most constant radiological finding was enlargement of one optic foramen, which occurred in 24 cases; in 2 cases both foramina were enlarged. In 5 cases no enlargement was seen, and in these the tumour was confined to either the orbit or the intracranial cavity; in 3 cases radiographs of the foramina were not obtained. Pneumography was performed in 21 cases because of suspected intracranial involvement, and in each case a suprasellar mass was found.

In the authors' view radical surgery usually causes an increase in the visual deficit which is permanent. In the majority of cases in the present series surgery was limited to verification of the lesion by gross inspection. In 2 cases the operation revealed that the optic chiasm was not involved, and consequently the optic nerve was divided proximal to the tumour; in 2 other cases a Torkildsen procedure was carried out, and in one a ventriculo-ureteral anastomosis was performed. The technique of radiation therapy was consistent in all cases, although the dosage and time of delivery varied. Patients treated before 1950 received three courses of irradiation, the tumour dose in each being 1,200 r in 8 to 21 days. The authors' present practice is to give 4,000 r over 28 days. The quality of the radiation varied between 0·95 mm. Cu and 1·2 mm. Cu H.V.L., 2 opposing fields being used in most instances.

When all the patients in whom optic glioma was diagnosed during the last 5 years were excluded, there remained 19 of the original 34 for follow-up assessment. Of these, 15 survived more than 5 years after irradiation was begun. In 8 cases there was arrest or improvement of the visual deficit which continued for 5 years. In 3 cases marked exophthalmos regressed completely.
E. D. Jones

1343. **Convergence Radiotherapy for Carcinoma of the Bronchus.** (Die Konvergenzbestrahlung des Bronchialkarzinoms)
L. Sieckel. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**. 970–973, June 15, 1956. 2 figs., 25 refs.

The convergent-beam technique makes it possible to give a tumour dose of 5,000 r at a depth of 11 cm. for a skin dose of no more than 1,000 r at any one point. Unfortunately, the full tumour dose is received by only a very small volume of tissue and falls off rapidly outside this zone; thus, truly uniform radiation of a pulmonary tumour is not possible by this method. Nevertheless, the author, working at Knappschaftskrankenhaus, Recklinghausen, Westphalia, has treated by this technique 66 patients with inoperable bronchial carcinoma in the last 4 years, of whom 19 are still alive. About half of these cases were referred by a thoracic surgeon as inoperable; the others were sent direct to the radiological department as inoperable on account of poor general condition or the advanced state of the growth. No fewer than 11 of the patients were over 70 years of age, and 28 were between 60 and 70. There was histological confirmation of the tumour in about one-quarter of the cases. No case in which the diagnosis was doubtful was included in the study.

The author divides his cases into five groups. (1) In the 6 cases in this group irradiation was palliative only, or for one reason or another incomplete, the tumour dose being no more than 3,000 r; the average survival time after treatment was 3 months. (2) Of the 27 patients in this group, 6 remain alive. These patients were treated in the first year of the study and received tumour doses of 3,000 to 4,000 r; the average survival time was 9·5 months. (3) The tumour dose in this group was 5,000 r, but because of poor condition or severe reaction to irradiation no second course was given; of the 12 patients, 2 are alive, the average survival time being 9 months. (4) Patients in the fourth group received two courses of irradiation at an interval of 3 months, the total tumour dose being 7,000 to 8,000 r; of the 9 treated in this way, 3 survive, the average survival time so far being 19 months. (5) The 12 patients in this

group received, in two or three courses of irradiation, between 10,000 and 15,000 r, and of these 8 remain alive, the average survival time so far being 10 months. The longest period of survival in this series has been 30 months after treatment. The author stresses that the palliative value of the treatment was very great, resulting in cessation of bleeding, re-expansion of collapsed lung, and a great improvement in the general condition of the patients.

Finally, the author discusses the question of preoperative radiotherapy. At this clinic preoperative courses of 5,000 r have been given without adding any difficulties to the operation, which, however, should follow as soon as possible after radiotherapy. He suggests that it may be advisable to give treatment with a stationary beam to the lymph drainage area in addition to the convergent-beam treatment of the primary growth.

E. Stanley Lee

1344. **Radiotherapy of Cancer of the Lung. Results in a Selected Group of Cases**

J. SMART and G. HILTON. *Lancet* [*Lancet*] **1**, 880–881, June 9, 1956. 7 refs.

The treatment of carcinoma of the bronchus has hitherto been regarded as primarily surgical, with or without radiotherapy, radiotherapy alone being reserved for inoperable cases. Hence while 5-year survival rates as high as 32% have been reported after surgery, the survival rate with radiotherapy alone at 5 years is consistently under 5%, patients being selected for such treatment only because of spread to the mediastinum or elsewhere. Having observed one patient with advanced disease who survived 13 years after radical *x*-ray therapy and 2 patients with localized disease similarly treated who survived more than 5 years without operation, the authors considered it justifiable to treat a small and selected group of cases of early bronchial carcinoma with radiotherapy only. Each patient had localized disease and was in good general condition.

So far, 33 such cases have been treated in 8 years. Squamous-celled carcinoma was present in 23 cases and anaplastic carcinoma in 6, the type not being determined in the remaining 4. Before irradiation measures were taken to improve the general condition, to remedy anaemia if present, and to eliminate sepsis. For treatment the patients were admitted to hospital if possible. In cases of squamous-celled carcinoma multiple fields were used, and for anaplastic tumours large fields to include the mediastinum. For the former type a dose of 5,000 to 5,500 r was given, and for the latter 4,000 to 4,500 r, usually over 7 to 8 weeks.

Of 12 patients treated over 5 years ago, 4 are still alive and well (3 squamous, one anaplastic), one survived for 3 years, 2 for 2 years or more, and 5 died within the first 2 years. These figures suggest that the results of radiotherapy may eventually bear comparison with those of surgery, particularly as there is no treatment mortality to compare with an operative mortality of 10%. Another advantage of radiotherapy is suggested by the fact that only 2 out of 18 patients developed cerebral deposits, clinical evidence suggesting that after surgery the incidence is much higher. Since it is known that many cases considered operable on clinical grounds are found to be inoperable at thoracotomy, it is probable that the authors' series contained cases which were more advanced than was evident and this must be taken into consideration in assessing the results.

I. G. Williams

1345. **Radiation Reactions in the Lung**

A. G. W. WHITFIELD, W. H. BOND, and W. M. ARNOTT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 67–86, Jan., 1956 [received April, 1956]. 17 figs., 40 refs.

The authors, after a review of the literature on damage to neighbouring healthy tissue during radiotherapy, describe 29 cases of damage to the lungs seen at the United Birmingham Hospitals. In 17 of these cases the changes followed *x*-ray treatment for carcinoma of the breast and in most of the others had followed "cervicothoracic baths" for the treatment of reticuloses, or of carcinoma of the thyroid, oesophagus, or bronchus. The interval between treatment and onset of symptoms, which was known in 21 cases, ranged from a few weeks to 4 months. The authors consider that these patients were significantly underweight compared with the average person of the same age and sex and suggest that this may be a factor in aetiology. The pathology and diagnosis are discussed; in severe cases treatment with antibiotics to limit secondary infection and with ACTH (corticotrophin) is recommended. The radiological appearances are described and illustrated, and brief histories of the 29 cases with the radiotherapeutic technique employed are given in an appendix to the paper.

E. Stanley Lee

1346. **The Lattice Method in Radiotherapy with Fast Electrons.** (Die Gittermethode bei der Strahlenbehandlung mit schnellen Elektronen)

J. BECKER, G. WEITZEL, and C. B. V. D. DECKEN. *Strahlentherapie* [*Strahlentherapie*] **99**, 213–220, 1956. 6 figs., 19 refs.

From the Czerny Hospital for Ray Therapy, Heidelberg, a sieve technique is described, in which electrons from a 15-MeV betatron were employed. Lead, 1 cm. in thickness, gives complete absorption; iron was used at first, but gives a higher surface dose. The openings were 7 mm. in diameter, with an open to closed area ratio of 4 to 6. As measured on a film, dosage became homogeneous at a depth of 3·5 to 4 cm., reaching 33%, compared with 93% for an open field. The great advantage of the method is that it can be used to treat subcutaneous tumours which have been previously heavily irradiated to skin tolerance (up to 6,000 r), even with atrophy, sclerosis, or telangiectasia. The authors report that the method has now been in use for one year and that regression has been obtained in 40% of such cases. A daily surface dose of about 550 r is given, to a total of 8,500 to 10,900 r.

J. Walter

1347. **Acute Myeloid Leukaemia after Radioactive-Iodine Therapy**

J. D. ABBATT, H. E. A. FARRAN, and R. GREENE. *Lancet* [*Lancet*] **1**, 782–783, May 26, 1956. 11 refs.

History of Medicine

1348. **Hospitals, Medical Care and Social Policy in the French Revolution**
G. ROSEN. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **30**, 124–149, March–April, 1956. Bibliography.

Before the French Revolution conditions of extreme poverty were normal for a substantial proportion of the people of France. Relief schemes operated only locally, and medical care was hampered by a chronic shortage of personnel. This state of affairs naturally engaged the attention of the philosophers of the " Age of Enlightenment ", some of whom proposed that relief measures be assumed as a social obligation. Many of their ideas found expression in a commission appointed in 1786 to study the Paris hospitals.

The severe winter and unsettled conditions of 1789 created widespread demands for relief among the poor, and in January, 1790, the Constituent Assembly appointed a Committee on Mendicity. Its members worked assiduously under the chairman, Liancourt, and by the end of the year drew up a draft plan for a complete national scheme of assistance, which advanced the claim of the poor to relief as a right, provided for free domiciliary medical care by State doctors, for the creation of new hospitals in cities, and for the nationalization of charitable resources, and even envisaged a scheme of social insurance. The proposals were, however, overtaken by an economic crisis which diverted attention to problems of urgent immediate relief and by the abolition of the *octroi*, the chief tax supplying the hospital funds on which the scheme relied. The Assembly made provision in the Constitution for public assistance but took no further action.

Shortly after its first meeting the Legislative Assembly of 1791 adopted a motion which amalgamated the earlier committee and the Committee on Health to form the Committee on Public Assistance. This, too, was overwhelmed with urgent specific requests and its much-delayed report—presented at a time of political crisis in June, 1792—was shelved. The report reiterated the right of the indigent to public assistance or work, and emphasized especially the need for medical care. Many of these proposals were to be affected by legislation of the Assembly which suppressed the religious orders staffing the hospitals and which encouraged quackery by abolishing medical teaching institutions.

The Assembly was replaced in September, 1792, by the National Convention, which operated public assistance through a continuation of the former committee and a sub-commission of the Committee of Public Safety. The need to look after the dependants of the troops engaged in repelling invasion on the frontiers and the difficult social conditions caused by the upheaval at home emphasized the desirability of a national system of public assistance. This was accomplished by a series of laws based on the constitutional recognition of assistance as " a sacred debt of society ". A law passed on March 19, 1793, established a basis for a " logically organized " national system of social assistance. It abolished charity and begging and provided work relief for the able and assistance for the infirm at home or in hospital. It envisaged the creation of a voluntary social insurance fund. Later decrees dealt in detail with special groups—the needy, expectant mothers (including the unmarried), orphans, foundlings, illegitimate children, and the aged—and provided for medical aid in each district. Yet another law promulgated in May, 1794, dealt with pensions and medical care for the poor in country and town—a reflection of the Jacobins' dependence on the support of the masses. This specifically abolished the words " alms " and " hospital " and provided only for domiciliary assistance and the appointment of 3 salaried doctors in each district who were to be provided with food supplies as well as medicines. Unfortunately, the funds were not forthcoming because of the war, and after the fall of Robespierre's party the Convention and the Directory returned to a modified version of pre-Revolutionary arrangements. Nevertheless, the attempts of the French revolutionaries to give every individual a " legal right to existence " and to institute a national system of social assistance were to have a profound influence on future social policy in France and other countries. *Geoffrey R. Pendrill*

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